The control of schistosomiasis

Report of a WHO Expert Committee

World Health Organization
Technical Report Series
728

World Health Organization, Geneva 1985
CONTENTS

Introduction .................................................................................................................. 7

1. Epidemiology .......................................................................................................... 8
1.1 The parasite ........................................................................................................... 8
1.1.1 Advances in characterization techniques ....................................................... 9
1.1.2 Principal Schistosoma species that infect man ................................................. 9
1.1.3 Longevity of the adult worm ........................................................................... 12
1.1.4 Other Schistosoma species infecting man ....................................................... 12
1.1.5 The relationship between parasites and their snail intermediate hosts ......... 12
1.1.6 Differentiation of cercariae that infect man ................................................... 13
1.2 The snail intermediate host .................................................................................... 13
1.2.1 Snail identification .......................................................................................... 13
1.2.2 Laboratory maintenance of snails ................................................................... 15
1.2.3 Snail ecology .................................................................................................... 16
1.3 Current distribution of schistosomiasis ............................................................... 16
1.3.1 Global aspects .................................................................................................. 18
1.3.2 Species-specific epidemiological characteristics ........................................... 21
1.4 Man-made water resources ............................................................................... 22
1.4.1 Environmental and socioeconomic changes .................................................. 22
1.4.2 Effects of major water impoundments and irrigation .................................... 24
1.4.3 Risk of schistosomiasis .................................................................................. 25
1.4.4 Importance of small impoundments ............................................................... 26

2. Disease due to schistosomiasis ............................................................................. 27
2.1 Schistosoma mansoni ......................................................................................... 28
2.1.1 Pathology ....................................................................................................... 28
2.1.2 Clinical manifestations ................................................................................... 30
2.1.3 Effect of treatment on disease ....................................................................... 32
2.2 Schistosoma haematobium ................................................................................. 33
2.2.1 Pathology ....................................................................................................... 33
2.2.2 Clinical manifestations ................................................................................... 35
2.2.3 Effect of treatment on disease ....................................................................... 37
2.2.4 Schistosoma intercalatum ............................................................................... 38
2.3 Schistosoma japonicum and Asian schistosomes that infect man ................. 38
2.3.1 Pathology ....................................................................................................... 38
2.3.2 Clinical manifestations ................................................................................... 39
2.3.3 Effect of treatment on disease ....................................................................... 40
2.3.4 Schistosoma mekongi .................................................................................... 41
2.3.5 A species of Schistosoma found in Malaysia ................................................ 41
2.4 Carcinoma and schistosomiasis ....................................................................... 41
2.5 Other conditions associated with schistosomiasis ......................................... 43
2.5.1 Bacteraemia due to Gram-negative bacteria .................................................. 43
2.5.2 Hepatitis B virus ............................................................................................ 43
2.5.3 Nutrition and schistosomiasis ....................................................................... 44

2.6 The immune response to schistosomiasis in man .............................................. 44
2.6.1 Humoral immune response ............................................................................ 44
2.6.2 Associations between disease and immunity ................................................. 45
3. Methods of control ................................................................. 45
  3.1 Health education ............................................................... 46
    3.1.1 Behaviour, morbidity, and recognition of symptoms .......... 46
    3.1.2 Health for all by the year 2000 ................................... 47
  3.2 Diagnostic techniques ..................................................... 48
    3.2.1 Stool examination techniques .................................... 48
    3.2.2 Urine examination techniques .................................... 49
    3.2.3 Indirect diagnostic techniques ................................... 50
    3.2.4 Miracidial hatching techniques .................................. 50
    3.2.5 Immunodiagnostic techniques .................................... 51
  3.3 Chemotherapy ............................................................... 51
    3.3.1 Metrifonate ............................................................ 53
    3.3.2 Oxamnique .................................................................. 54
    3.3.3 Praziquantel .............................................................. 55
    3.3.4 Combination drugs ..................................................... 56
    3.3.5 Drugs under development .......................................... 57
    3.3.6 Resistance to drugs .................................................. 58
  3.4 Snail control ................................................................. 58
    3.4.1 Available molluscicides ............................................. 59
    3.4.2 Molluscicides under development ................................ 59
    3.4.3 Toxicity, mutagenicity, and carcinogenicity testing ......... 60
    3.4.4 Resistance to molluscicides ....................................... 60
    3.4.5 Laboratory screening of molluscicides ......................... 61
    3.4.6 The market for molluscicides ..................................... 61
    3.4.7 Mollusciding costs ................................................... 61
    3.4.8 Future role of molluscides in schistosomiasis control ..... 62
    3.4.9 Biological control .................................................... 62
  3.5 Environmental management and modification ....................... 63
    3.5.1 Irrigation schemes ................................................... 63
    3.5.2 Natural habitats ...................................................... 64
    3.5.3 Man-made reservoirs ................................................ 64
    3.5.4 Environmental modification ....................................... 65
  3.6 Sanitation and water supply ............................................. 65
    3.6.1 Sanitation ............................................................... 65
    3.6.2 Water supply .......................................................... 66
  3.7 Data management ........................................................... 67
    3.7.1 Requirements for data analysis in the control of schistosomiasis 67
    3.7.2 Sources of the information necessary for the preparation and implementation of control ............... 68
  3.8 Training ................................................................. 69
  4. Review of progress in national programmes .......................... 70
    4.1 Countries where S. mansoni is endemic ............................ 70
      4.1.1 Brazil ................................................................. 70
    4.2 Countries where S. haematobium is endemic ..................... 72
      4.2.1 Congo ................................................................. 72
      4.2.2 Morocco .............................................................. 73
      4.2.3 Tunisia ............................................................... 74
      4.2.4 United Republic of Tanzania: Zanzibar ....................... 75
    4.3 Countries where both S. haematobium and S. mansoni are endemic .... 76
WHO EXPERT COMMITTEE ON THE CONTROL OF SCHISTOSOMIASIS

Geneva, 8–13 November 1984

Members

Professor M.A. Amin, Ministry of Health and Social Welfare, Khartoum, Sudan
Professor Z. Andrade, Gonçalo Moniz Research Centre, Oswaldo Cruz Foundation, Salvador, Bahia, Brazil
Dr S.M. El Hak, Endemic Diseases Control Department, Ministry of Health, Cairo, Egypt
Dr P. Jordan, Medical Research Council, National Institute for Medical Research, London, England
Professor Mao Shou-Pai, Institute of Parasitic Diseases, China National Centre for Preventive Medicine, Shanghai, People's Republic of China
Professor E.H. Michelson, Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, School of Medicine, Bethesda, MD, USA (Rapporteur)
Professor A.B. O.O. Oyediran, Department of Preventive and Social Medicine, College of Medicine, University of Ibadan, University College Hospital, Ibadan, Nigeria
Professor A. Prata, Department of Tropical Medicine and Nutrition, University of Brasilia, Brasilia, Brazil (Chairman)
Dr D.H.G. Wegner, formerly, Medical Department, Bayer Pharma Research Centre, Wuppertal, Federal Republic of Germany

Representative of other organizations

Dr B. Liese, Population, Health and Nutrition Department, The World Bank, Washington, DC, USA

Secretariat

Dr J.A. Cook, Program in Tropical Disease Research, The Edna McConnell Clark Foundation, New York, NY, USA (Temporary Adviser)
Dr A. Davis, Director, Parasitic Diseases Programme, WHO, Geneva, Switzerland
Professor E.G. Garcia, Department of Parasitology, Institute of Public Health, University of the Philippines, Manila, Philippines (Temporary Adviser)
Dr N. Katz, Laboratory for Schistosomiasis, René Rachou Research Centre, Oswaldo Cruz Foundation, Belo Horizonte, Minas Gerais, Brazil (Temporary Adviser)
Dr K.E. Mott, Chief, Schistosomiasis and other Trematode Infections, Parasitic Diseases Programme, WHO, Geneva, Switzerland (Secretary)
THE CONTROL OF SCHISTOSOMIASIS

Report of a WHO Expert Committee

A WHO Expert Committee on the Control of Schistosomiasis met in Geneva from 8 to 13 November 1984. Dr S.K. Litvinov, Assistant Director-General, opened the meeting on behalf of the Director-General.

INTRODUCTION

During the five years since the meeting of the WHO Expert Committee on the Epidemiology and Control of Schistosomiasis (19) there have been changes in the priorities and operational approaches adopted, since the immediate aim is now to control the morbidity due to schistosomiasis rather than to control its transmission. Advances have occurred in parasitological diagnostic techniques, chemotherapy, and our understanding of the human ecology and epidemiology of schistosomiasis, and this new knowledge is being incorporated into national control programmes.

Programmes to eradicate schistosomiasis or eliminate its transmission by multiple, integrated, intervention techniques are proving to be beyond the human and financial resources of most endemic countries and the objectives of such programmes will only be achieved in the long-term. However, a reduction in disease due to schistosomiasis is now a feasible objective that is based on sound epidemiological principles and it is an objective that can be achieved within the limitations of most endemic countries. Since the epidemiology of schistosomiasis varies from one endemic country to another, the managerial and operational structures of schistosomiasis control programmes will also vary. The simplicity of the diagnostic techniques, the safety and ease of administering oral anti-schistosomal drugs, the use of snail control measures based on specific epidemiological criteria, and precise methods of data collection and analysis, mean that schistosomiasis control activities can be adapted to suit any level of the health care delivery system. In primary health care programmes, it can now be safely anticipated that schistosomiasis control activities to reduce morbidity will be successful.
The strategy of morbidity control focuses on the population of an endemic country. Schistosomiasis is caused by the insanitary habits of man. Schistosomiasis is acquired by man as he performs necessary daily activities associated with fresh water—working, bathing, washing, fishing, and recreation. The disease condition related to schistosomiasis is caused by heavy infections. Health education as part of morbidity control is important in helping the population to modify behaviour to prevent the disease, to understand the meaning of health in contrast to disease, to recognize the symptoms of schistosomiasis, and to use appropriately the available health facilities; health education should also encourage community involvement in control programmes with a view to social action.

The success of intervention measures that have a direct impact on morbidity such as chemotherapy, water supply and sanitation, environmental management, and environmental modification all require the active participation of the population. The new approach to schistosomiasis control emphasizes collaboration and implementation at the primary health care level in preference to the combined use of different intervention methods.

The Expert Committee recognized that the organizational, managerial, and operational aspects of control are the major areas where progress can be made in the future.

This report stresses the importance and feasibility of reducing morbidity in schistosomiasis control programmes using available methods and resources.

1. EPIDEMIOLOGY

1.1 The parasite

Much of the recent work on the taxonomy of schistosome parasites has focused on the use of experimental methods to assist in the characterization of species and strains. The need to define and identify accurately schistosome genotypes has stimulated this research. Many observations, both in the field and in the laboratory, have shown that strains of a single species from different geographical areas may display marked differences in their biological characteristics, implying that genetic diversity exists within the genus *Schistosoma*. 

8
The intraspecific variation that has been reported includes differences in minor morphological characteristics, infectivity to snails, periodicity of cercarial emergence, response to drugs, ability to develop in different definitive hosts, growth rates, egg production, prepatency periods, pathogenicity, and immunogenicity. To complement these observations, studies on enzymes, chromosomes, and DNA have been carried out in attempts to find markers that can be used to identify species and strains and to assess inter- and intraspecific relationships.

1.1.1 Advances in characterization techniques

(1) Enzyme electrophoresis. Recent technical improvements in both starch-gel and isoelectric focusing in polyacrylamide gels have meant that several instead of single enzymes from individual schistosomes can be studied, thus allowing a genetic interpretation of the results.

(2) DNA. Advances in molecular biology have provided new methods of identification. Cloned DNA sequences from the genome of Schistosoma mansoni encoding portions of the ribosomal RNA gene have been found to differentiate readily between adult worms and the cercariae of S. mansoni, S. haematobium, and S. japonicum as well as between various strains of S. mansoni.

(3) Chromosomes. Recent improvements in the study of chromosomes have occurred with the perfection of a technique for air-drying the specimen prior to staining with Giemsa and with the use of C-banding techniques that have been particularly valuable in distinguishing sex chromosomes.

(4) Snail compatibility studies. In an attempt to quantify the degree of compatibility between schistosomes and their snail hosts, an index has been proposed that involves the evaluation of cercarial production.

1.1.2 Principal Schistosoma species that infect man

Of the 16 species of schistosomes known to infect man or animals (I2), the 5 principal ones are dealt with here and 11 others are mentioned in section 1.1.4 on page 12. The 5 principal species that infect man fall into one of three groups that are characterized by the type of egg produced: (a) eggs with a lateral spine, e.g., S. mansoni; (b) eggs with a terminal spine, e.g., S. haematobium and
S. intercalatum; and (c) eggs that are round and minutely spined, e.g., S. japonicum and S. mekongi.

Schistosomes similar to S. mansoni have been found in rats (S. rodhaini) and numerous S. haematobium-like parasites with terminal-spined eggs have been found in a variety of animals and occasionally in man, e.g., S. bovis and S. mattheei in southern Africa.

1.1.2.1 Schistosoma mansoni. This is the only species with a lateral-spined egg that infects man. The female worm of this species produces 100–300 eggs or more per day.

Isolates of S. mansoni from different geographical areas show marked differences in their ability to develop in the various species and strains of the snail genus Biomphalaria. In South America, strains of S. mansoni have been isolated that seem to be adapted to particular snail hosts. When a comparison is made between a strain adapted to B. glabrata and one adapted to B. tenagophila, differences are found in the length of the adult worms, in the size of the eggs, and in the prepatent period within the snails. Each snail population has been found to be susceptible to its own particular strain of parasite, but is virtually refractory to infection with any other strain.

So far no particular characteristic of the parasite has been related to any specific clinical manifestation.

1.1.2.2 Schistosoma haematobium/Schistosoma intercalatum. These two species have terminal-spined eggs. A S. haematobium female worm produces 20–200 eggs per day; the fecundity of S. intercalatum is unknown.

Isolates of S. haematobium from Africa and adjacent regions can display marked differences in infectivity to various species of the snail genus Bulinus. In general, S. haematobium in Africa south of the Sahara is transmitted by snails of the Bulinus africanus group, in the Mediterranean area and South-West Asia by tetraploid members of the B. tropicus/truncatus complex, and in Arabia and Mauritius by members of the B. forskali group. In West Africa, all three snail groups are known to act as hosts for S. haematobium. Of particular significance is the major division between the northern, B. truncatus-borne S. haematobium and the B. africanus-group-borne parasites; with few exceptions, neither of these forms can develop in the snail host of the other.

A new animal model for S. haematobium infection has been identified and involves the use of Erythrocebus patas (African red
monkey). This new model system may prove to be both more efficient and less expensive than the use of baboons.

Intestinal schistosomiasis in man caused by *S. intercalatum* is endemic in parts of Cameroon, Gabon, and north-east Zaire, and possibly other parts of Central and West Africa. Two strains are known that are not cross-infective: one is transmitted by snails belonging to the *Bulinus africanus* group in parts of Zaire, while the other is transmitted by *B. forskali* in Cameroon and Gabon.

Natural hybrids between *S. haematobium* and *S. intercalatum* have been found in Loum, Cameroon. Over a ten-year period, the number of cases of intestinal schistosomiasis caused by *S. intercalatum* has markedly decreased, whereas the number of cases of urinary schistosomiasis caused by *S. haematobium* and the hybrid parasite has increased. The laboratory hybrid between *S. haematobium* and *S. intercalatum* has been found to exhibit heterosis by its enhanced infectivity to both snail hosts and experimental animals as well as by an increased growth rate and reproductive potential.

1.1.2.3 Schistosoma japonicum/S. mekongi. Each female worm of *S. japonicum* produces 500–3500 eggs per day; no estimate has yet been made of the fecundity of *S. mekongi*. Few studies have been carried out in recent years relating directly to the characterization of strains of *S. japonicum*. This species group has a very wide natural definitive host range. In some endemic areas, natural infection with *S. japonicum* has been shown to occur in at least 31 mammalian species, whereas natural *S. mekongi* infection has been reported only in dogs and man.

Differences between *S. mekongi* and one or all of the known strains of *S. japonicum* from different geographical areas, have now been documented and include the morphology of the egg, miracidium, and adult worm. *S. mekongi* exhibits a greater virulence in experimental rodents whereas its virulence in dogs appears to be less than that of *S. japonicum*. The aquatic snail *Tricula aperta*, the snail host for *S. mekongi*, is not compatible with *S. japonicum*; similarly, the various geographical strains of amphibious *Oncomelania hupensis*, the snail host for *S. japonicum*, are not compatible with *S. mekongi*. 

11
1.1.3 Longevity of the adult worm

Although there are individual reports that adult schistosome worms may live for several decades (9), epidemiologically derived estimates suggest that the average life-span is about 5 years for *S. japonicum*, *S. mansoni*, and *S. haematobium*.

1.1.4 Other Schistosoma species infecting man

In addition to the 5 schistosome species known to infect man, another 11 zoophilic species have been recognized. It is important that these parasites are studied since any species that lacks definitive host specificity might prove to be a potential health hazard, especially if there is a possibility that it might hybridize with a known human parasite. In southern Africa, *S. mattheei*, a parasite of cattle but with a wide host range, is known to develop in man in the presence of *S. haematobium* and/or *S. mansoni*. Initial observations on the egg morphology of this species suggest that hybridization occurs between *S. haematobium* and *S. mattheei*. There is speculation that the *S. mattheei/S. haematobium* hybrid may pose a health threat to man. It is possible that the incidence of infection with *S. mattheei*-like parasites in man might increase and a hybrid might evolve that is capable of infecting either man or cattle with equal ease. It has been suggested that the poor response of *S. mattheei* to oxamniquine treatment may be due to its hybridization with *S. haematobium*. Clearly, the potential health hazard posed by this hybrid should be closely monitored.

A parasite resembling *S. japonicum* that is transmitted by *Robertiella kaporensis* in Malaysia, has been found to infect man (5) (see section 2.3.5).

1.1.5 The relationship between parasites and their snail intermediate hosts

Studies on the relationship between species and strains of parasite and their actual and potential snail hosts have revealed considerable variation in infection rates, duration of infection, cercarial production, and snail mortality. Such differences are due, not only to differences in the susceptibility of the snail species but also to the infectivity of the parasite.

Compatibility between parasite and snail intermediate host is largely determined by genetic factors and snails may be refractory
or susceptible. Susceptibility may be influenced by ecological and other biological parameters.

The susceptibility of the snail to infection affects the number of cercariae released, and this number may vary from day to day. The size of the snail host is an important factor in determining the output of the snail. An example of a peak of cercarial production is that up to 3000 *S. mansoni* cercariae may be released daily from highly susceptible *Biomphalaria* spp. snails. From large *Bulinus* spp. snails, 2000 *S. haematobium* cercariae may be released per day. The majority of the cercariae of *S. mansoni* and *S. haematobium* are shed by the snails around midday, but the small number of *S. japonicum* cercariae, usually only about 15 per day (associated with the small size of the snails of *Oncomelania hupensis* subspp.) are shed at night and survive for 24 hours.

1.1.6 *Differentiation of cercariae that infect man*

At present, although laboratory techniques may be used to identify some schistosome cercariae, they cannot be used in the field for epidemiological cercariometric studies, so problems may arise in waters where schistosomes that infect man and animals are mixed.

1.2 *The snail intermediate host*

The snail intermediate host is an essential link in the life-cycle of the schistosome parasite. An adequate knowledge of its taxonomy, genetics, physiology, distribution, and ecology is necessary if its role in transmission is to be interpreted correctly.

1.2.1 *Snail identification*

The identification of snails is essential if the transmission and control of schistosomiasis is to be understood. Classical methods (comparative morphology of shells, radula preparations, and soft anatomy, especially of the genitalia), are still adequate to separate schistosome-bearing snails from other aquatic snails in areas where only one host occurs, e.g., *Oncomelania hupensis quadrasi* transmitting *S. japonicum* in the Philippines, or *Biomphalaria glabrata* transmitting *S. mansoni* on St Lucia. These methods may also be adequate where two hosts are involved (e.g., *Biomphalaria glabrata* and *Biomphalaria straminea* transmitting *S. mansoni* in
Brazil, or *Bulinus globosus* and *Bulinus truncatus rohlfsi* transmitting *S. haematobium* in Ghana). Simple regional keys have been produced for Africa, the Eastern Mediterranean region, and South America (3, 7, 14).

Chromosome counts made on ovotestis and embryonic tissues have provided additional information to clarify the relationships among the bulinids. The use of chromatograms of surface mucus, which is a promising technique for European lymnaeids, has proved to be less satisfactory for either *Bulinus* spp. or *Biomphalaria* spp. snails. Electrophoresis of muscle and egg proteins is more promising and the sensitivity of this technique may be improved by the additional use of isoelectric focusing.

Recently, attention has turned to the use of enzyme and isoenzyme analysis to characterize the species of *Bulinus* and *Biomphalaria*. The interpretation of these analyses, regarding the number of enzymes and individual snails required and the possible effects of parasites, commensals, and diet on isoenzyme patterns, has caused some controversy. Isoenzyme markers of susceptibility have been reported in *Biomphalaria glabrata*. It is now feasible to isolate genes coding for specific isoenzymes; thus, using genetic engineering techniques, very specific molecular probes may be developed for use in relatively simple immunodiagnostic techniques. However, these more advanced taxonomic methods are likely to be restricted mainly to well-equipped laboratories. There is some risk that distorted results may be produced if differential mortality occurs among the taxonomic variants during the transport of living material from the tropics to the laboratory.

(1) Snail hosts of *S. japonicum*. The status of snail hosts of *S. japonicum* and other closely related species was reviewed by the last Expert Committee (19). *S. japonicum* is transmitted by the polytypic species *Oncomelania hupensis*. On the Chinese island of Taiwan, strains of *O. h. formosana* and *O. h. chiai* transmit the local zoophilic strain of *S. japonicum*, but some strains are also susceptible to foreign human *S. japonicum* strains. Knowledge of the distribution of the snail hosts on the island would be relevant should the human parasite be introduced.

*S. mekongi* found in the Mekong river area is transmitted by polytypic *Tricula aperta*. In Malaysia, a parasite resembling *S. japonicum* is transmitted by the hydrobiid snail, *Robertsiella kaporensis*.

14
(2) Snail hosts of S. haematobium. Although considerable progress has been made (employing karyotype analysis and electrophoretic techniques) in the study of the taxonomy of African bulinid snails, our understanding of species relationships and the susceptibility of populations of closely related species is far from satisfactory. At present, our knowledge of the various species that act as actual or potential hosts is essentially the same as was presented in the report of the last Expert Committee (19). The role of Bulinus forskali as a host for S. haematobium remains suspect; however, this species is capable of transmitting S. bovis, S. intercalatum, and possibly S. haematobium/intercalatum hybrids. Recent evidence suggests that Planorbarius metidensis is not a host of S. haematobium in North Africa and its importance as a host in other areas bordering on the western Mediterranean area can probably be ignored.

(3) Snail hosts of S. mansoni. The taxonomic status of both African and Neotropical Biomphalaria spp. is better defined than is the case for the African bulinids. The comments of the last Expert Committee (19) are still relevant and recently information concerning the African Biomphalaria spp. has been updated (3). Variations in the compatibility of biomphalard species and populations to both sympatric and allopatric strains of the parasite continue to be recognized. Although Biomphalaria straminea is the most widely distributed species in the Neotropics, it serves as a host only in Brazil. Studies on the biology, ecology, and capacity to transmit infection of this species should be extended. Recent recognition of a new Neotropical species, B. occidentalis, which is not susceptible to infection and which can be distinguished only by internal morphology from B. tenagophila, may necessitate a re-evaluation of both S. mansoni transmission in southern Brazil and the risk of the infection spreading into the western area of the country. Similarly, B. amazonica, which has been recently identified from Amazonia and found to be susceptible to infection in the laboratory, may pose a problem in this area.

1.2.2 Laboratory maintenance of snails
The many papers published on the subject provide evidence of the ease with which S. mansoni can be maintained in the laboratory in Biomphalaria glabrata, compared with other Schistosoma spp.
Procedures vary among laboratories, but high-protein supplements (e.g., fish and mammal foods) are widely considered to be necessary for the maintenance of snail colonies. Even so, periodic catastrophes occur in *B. glabrata* colonies; these are usually due to the accidental introduction of harmful chemical or biological agents. However, because it is more difficult to maintain other *Biomphalaria* spp., there have been instances where specimens of *B. glabrata* have been imported, by research laboratories, into areas outside the natural range of the species but in which schistosomiasis is endemic. The introduction and maintenance of snail intermediate hosts, particularly *B. glabrata*, in non-autochthonous areas is not recommended.

In the past, difficulties in the large-scale laboratory culture of *Oncomelania* spp. restricted work on *S. japonicum*; however, it is now possible to produce large numbers of *Oncomelania hupensis hupensis* and provide parasite material for laboratory studies. *Tricula aperta*, the intermediate host of *S. mekongi*, can also be kept in the laboratory.

The large-scale maintenance of *Bulinus* spp., and hence *S. haematobium*, remains difficult. Loss of parasite infectivity after several passages through laboratory hosts and the development of snail resistance are recurrent problems. Occasionally the cycle has been maintained for more than a few generations without replenishment of the snail and/or the parasite from endemic areas, but usually there is insufficient material for experimental studies. Only rarely has a chance combination of snail and parasite permitted prolonged, reliable production on the scale needed for experimental studies. A similar situation exists for other terminal-spined schistosomes.

1.2.3 Snail ecology

The report of a previous WHO Expert Committee (19) stressed the need for additional studies to be made on snail ecology. This remains the case and the comments of the previous Expert Committee are still relevant and should be consulted.

1.3 Current distribution of schistosomiasis

Of all the parasitic infections that affect man, schistosomiasis is one of the most widespread. In terms of socioeconomic and public health importance in tropical and subtropical areas, it is second only
Fig. 1. Global distribution of schistosomiasis due to Schistosoma haematobium, S. japonicum, and S. mekongi*  

*S. haematobium

*S. japonicum

*S. mekongi

*The original version of this map was prepared by Ch. Cheung.
Fig. 2. Global distribution of schistosomiasis due to *Schistosoma mansoni* and *S. intercalatum*.

*The original version of this map was prepared by Ch. Chaung.*
<table>
<thead>
<tr>
<th>Country or area</th>
<th>S. mansoni</th>
<th>S. haematobium</th>
<th>S. intercalatum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>African Region</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Algeria</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Angola</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Benin</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Botswana</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Burundi</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cameroon</td>
<td>+</td>
<td></td>
<td>+*</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chad</td>
<td>+</td>
<td></td>
<td>+*</td>
</tr>
<tr>
<td>Congo</td>
<td>+</td>
<td></td>
<td>+*</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabon</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Gambia</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ghana</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea-Bissau</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivory Coast</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liberia</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Madagascar</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malawi</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mali</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mauritania</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mauritius</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mozambique</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Namibia*</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Niger</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nigeria</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rwanda</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sao Tome and Principe</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senegal</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swaziland</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Togo</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uganda</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Zaire</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Zambia</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Region of the Americas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antigua</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guadeloupe</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martinique</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montserrat#</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saint Lucia</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suriname</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venezuela</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Eastern Mediterranean Region</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Democratic Yemen</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iran, Islamic Republic of</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iraq</td>
<td>+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\* Data unavailable or insufficient.
\# Data unavailable or insufficient.
to malaria. It is one of the main occupational risks encountered in the rural areas of developing countries, and is second to none in prevalence among water-borne diseases.

1.3.1 Global aspects

Schistosomiasis is now endemic in 74 countries of the world (see Table 1 and Fig. 1 and 2). It is estimated that more than 200 million persons residing in rural and agricultural areas are infected and that between 500 and 600 million persons are exposed to infection because of poverty, ignorance, poor housing, substandard hygienic practices, and the availability of few, if any, sanitary facilities.

In the past, *S. japonicum* infection in man has occurred in six countries; but it is found today only in China, Indonesia, and
the Philippines. Infection with *S. mekongi*, a close relative of *S. japonicum* has been found in two South-East Asian countries. *S. haematobium* is endemic in 52 eastern Mediterranean and African countries. *S. mansoni* infection occurs in 53 countries from the Arabian peninsula to Brazil, Suriname, Venezuela, and certain Caribbean islands. In 40 countries, both *S. mansoni* and *S. haematobium* are reported to be endemic. *S. intercalatum* causes a form of human intestinal schistosomiasis that has been reported infrequently from 6 central African countries. This form of schistosomiasis is now being diagnosed more frequently, however.

*S. haematobium* infection has recently been reported in an area of agricultural development associated with irrigation in Sao Tome and Principe. *S. mansoni* infection has now been reported from Niger and Oman.

1.3.2 *Species-specific epidemiological characteristics*

The epidemiology of schistosomiasis is not necessarily uniform within an endemic country and it cannot be compared between countries. Water-resource development projects for irrigation and agricultural purposes can change the epidemiology in an endemic area from seasonal and highly focal transmission of schistosomiasis to intense, widespread, and constant transmission.

(1) *S. mansoni*. In most areas endemic for *S. mansoni* the prevalence of infection is generally greatest in the 10–24-year-old age group. Prevalence in older age groups tends to remain at high levels compared with the usual prevalence curve of *S. haematobium* infection. A small proportion (5–25%) of the infected population excretes at least 50% of the total number of eggs contaminating the environment. Most of these heavily infected persons are between 10 and 14 years of age. A high proportion of children with elevated *S. mansoni* egg counts (> 800 eggs per gram of faeces) have enlarged livers and spleens.

(2) *S. haematobium*. A considerable amount of epidemiological data has become available from well-defined communities where *S. haematobium* is endemic. The peak prevalence and intensity of infection generally occur in children aged between 10 and 14 years, with a low prevalence and intensity of infection in the older age groups. In general, 60–70% of all infected persons are 5–14 years of age; the most heavily infected persons are also in this age group.
In children and adults increasing levels of haematuria and proteinuria are associated with increasingly heavy *S. haematobium* infections. Cystoscopic, renographic, and radiological changes of the urinary tract are associated with heavy infections in children. In several studies, haematuria was detected using reagent strips in nearly all children (98–100%) with more than 50 *S. haematobium* eggs per 10 ml of urine. Among all infected children in different endemic areas, 80% were found to have haematuria.

(3) *S. japonicum*. There is no typical age prevalence and intensity distribution of *S. japonicum* infection and this reflects the variations in epidemiology from one area to another. Bimodal age prevalence curves with peaks in the 10–14 years and 35–44 years age groups have been reported.

1.4 Man-made water resources

1.4.1 *Environmental and socioeconomic changes*

In many areas, water-resources development projects tend to cause some degradation of the environment through the destruction of forest galleries, increased soil erosion, and the production of more favourable biotopes for the intermediate hosts of the schistosomes and vectors of other parasitic or infectious diseases. The construction of new dams is imperative, but inevitably they affect the environment and health of the population.

The inhabitants of localities where there are man-made water-resource development projects are affected by economic and social disturbances. Resettlement programmes, when properly implemented, may minimize these problems.

The movement of populations as a result of actual or possible opportunities for work during the construction of water development projects can aggravate the local conditions of life because of housing difficulties, overcrowding, rising costs of living, and other social problems. These migrations may also introduce new sources of disease or even new diseases as well as persons who are immunologically susceptible to the diseases endemic in the area of development.

The existence of adequate health services and of an infrastructure for the control of endemic diseases, can, in certain areas, reduce or eliminate specific risks and result in an improvement in general
health. However, the less dramatic problems will probably remain unnoticed, and the changes that are slow to develop such as those dependent on eutrophication, on cumulative pollution, or on the deterioration of human living conditions may not be considered. Many of these detrimental changes can be prevented more economically than by the provision of curative medicine. If preventive measures are implemented sufficiently early, they will require fewer personnel, less equipment, and less material than if the breeding areas of disease vectors or intermediate hosts are allowed to develop and the prevalence rates of diseases to increase.

In addition, the necessary protection of the environment to maintain the quality of water and to eliminate most of the health risks associated with water development projects also requires that adequate use be made of the land. This means that the use of the land around the impoundment, the establishment of new settlements, and the industrial, agricultural, and other activities should be planned and regulated in accordance with ecological principles and sanitary and social interests. This type of planning is the most economical and efficient way of preventing or controlling health risks, and of improving the quality of life in the area. One of the purposes of planning is to ensure that a reasonable part of the investment and of the benefits produced by the water-resources development project is administered in such a way that local development can be financed and guided adequately.

The risk of the spread of parasitic infections has been stressed on many occasions. Some of these warnings are contained in documents prepared during the planning stages of particular schemes, others are found in reports dealing more generally with the health hazards of water development (10).

It is to be expected that the group of infections described as water-related will become increasingly prevalent as the uncontrolled use of water increases. Schistosomiasis stands out for a number of reasons: (a) an increase in disease prevalence associated with a greater use of water in endemic areas has been observed in many countries in Africa that are currently engaged in water development schemes; (b) this phenomenon has been observed simultaneously across the whole African continent; (c) these increases in prevalence have often been extremely high, are relatively easy to detect, and have frequently caused a public outcry because of the presence of a dramatic sign of the infection, e.g., intense haematuria in a large proportion of the children. In contrast, if an increase in the prevalence of other
parasitic infections has occurred as a result of closer contact with water, it has apparently been more localized, not so readily associated with the cause, and probably less dramatic.

1.4.2 Effects of major water impoundments and irrigation

Relatively few comparisons have been made between disease distribution and intensity in areas before and after development but those available are concerned almost exclusively with schistosomiasis. Outlined in this section are examples of the experiences of some countries.

(1) Egypt. Construction of the Low Dam at Aswan in the early 1930s allowed perennial irrigation in a number of provinces in Egypt. This was followed by an increase in *S. haematobium* infections between 1934 and 1937 in the four areas that were investigated; existing levels of prevalence (from 2 to 11%) rose to 44–75%.

Associated changes in schistosomiasis transmission patterns have occurred in both Upper and Lower Egypt. In the Nile Delta, *S. mansoni* is now the predominant species and is rapidly spreading throughout the Nile river area. Although these changes appear to have occurred in association with the construction of the High Dam at Aswan, no causal effect has been proved. *Biomphalaria alexandrina*, the intermediate host of *S. mansoni* in Egypt, has now spread via the Nile to the Aswan Governorate.

(2) Sudan. Irrigation of the Gezira by the construction of the Sennar Dam in 1924 and extension of the irrigation system after 1950 have resulted in a progressive increase in schistosomiasis. The prevalence of *S. haematobium* infection rose from less than 1% in the period 1924–44 to 21% in adults and 45% in children in 1952. *S. mansoni* prevalence rates were 5% in 1947, and between 77% and 86% in the 7–9-year-old age group in 1973.

(3) West Africa. Large-scale surveys for cases of urinary schistosomiasis were undertaken covering much of Ghana in the decade before the Akosombo Dam was built. Low prevalence rates (5–10% in children) were found around the area that was later impounded. In 1968, within a year of Lake Volta reaching its maximum level, very high prevalence rates (over 90% in children aged 10–14 years) were found in some lakeside communities. There are approximately 150 000 people living along the lakeshore.
Further proof of the effects of Lake Volta was provided by a study of disease prevalence in communities situated away from the lake. The prevalence rates fell progressively along a transect of 7 km from the lake and were directly related to a decreasing degree of dependence on the lake for domestic water.

Schistosomiasis infection is expected to increase in West Africa as a result of water development projects that have been encouraged by the disastrous Sahelian drought. Some of these projects are: Selingue dam, Mali; irrigation project of Gorgol, Mauritania; Sovapiti dam, Guinea; Mano river scheme, Sierra Leone; and Kandadjì dam, Niger.

1.4.3 Risk of schistosomiasis

Schistosomiasis affects three different population groups as a result of water-resource development schemes: (a) the autochthonous population; (b) workers and their families; and (c) migrants. Efforts to control schistosomiasis should include provisions for the diagnosis and treatment of all these groups.

Schistosomiasis transmission may already be established among the autochthonous population of the development area. Selective chemotherapy of this population at the very early stages of implementation may be more cost-effective than attempting to intervene at a later stage. If schistosomiasis is initially absent, subsequent surveillance of this population group will provide a sensitive indicator of its introduction.

The workers who are employed in the water-resource development project and their families should be screened and treated if infected. The provision of adequate community services, including especially water and sanitation, will help control schistosomiasis as well as other infectious and parasitic diseases.

During the planning phase of the project, predictions are usually made of the level of population migration into the area. If it is assumed that the new population will come from an endemic area, a programme of screening and treatment in health facilities in the area of origin and/or in the project area may prevent the introduction of schistosomiasis or of new species of schistosomes into the project area.

Public awareness of schistosomiasis may emerge slowly because the onset of the disease is usually insidious and the appearance of grosser clinical manifestations slow. Depending on the intensity of
infection, the full manifestations of the severe disease may develop more rapidly if there is explosive transmission as the result of a new water development project.

1.4.4 Importance of small impoundments

Scientific attention has focused on major water impoundments in the tropical world that are not only important as problems in their own right but also have symbolic value for human achievement. However, it is likely that small water impoundments, when considered together, have an equally great or even greater impact on human health.

Although comprehensive data are not available, it seems certain that the rate of construction of small dams is increasing rapidly. One reason for this increase, apart from improved knowledge of agronomic and hydrological techniques and from the accruing production benefits, is the "bulldozer revolution"; the ready availability of earth-moving equipment for purchase, loan, lease, rent, or shared ownership has led to a considerable earth-moving capability at local community levels. The results are that in addition to government-supported agricultural projects, village communities, farmer cooperatives, and other agencies in the tropical world can, on their own initiative, construct small water impoundments.

Without denying their agricultural benefits, the small impoundments are hazardous to health since they are associated with a high risk of disease transmission and are usually constructed without any provision of health care measures. Furthermore, small impoundments, especially when they are not financed by the government, are often affected by problems of maintenance, sewage, and water discipline, all of which favour an increase in schistosomiasis transmission.

In the Upper Region of Ghana about 120 small dams are being constructed with foreign aid. Recently, technical assistance has been proposed for the construction of the 20 dams needed to support an agricultural programme in the Northern Region of the country. In Nyanza Province of Kenya, where a programme of small dam construction began in 1957, 50,000 dams were built within three years. In Mali, to promote vegetable growing, a series of 50 small dams is being constructed in the district of Bandiagara which has a population of 160,000. By 1977 about 20 of these dams had been completed or were under construction (10).
Information on national programmes for the construction of large and medium impoundments is easier to obtain than is similar information for small dams; the larger impoundments are fewer, require central funds and other resources, and are often associated with a national objective, while small dams are usually built according to local needs, decisions, and inputs.

The demand for food and energy in most developing countries suggests that the need for small water-resource development in areas where schistosomiasis is endemic is unlikely to decrease. Relevant government departments and local authorities should be made aware of the potential health hazards involved and should be encouraged to register existing and new impoundments and to develop regulations and integrated planning strategies for the implementation of preventive health measures. These may have to be modified and adapted from the integrated planning strategies developed for major impoundments.

2. DISEASE DUE TO SCHISTOSOMIASIS

From standard textbooks of clinical medicine, it might be assumed that there is little new information on the pathology and clinical manifestations of schistosomiasis. On the other hand, our understanding of the pathology of schistosomiasis has been enhanced by the use of quantitative tissue digestion techniques which provide an assessment of tissue egg burden, as well as by the use of immunopathological techniques to study the basic pathological mechanisms in man. In addition, pathologists have become increasingly aware of the need to use a baseline population as a reference for their results.

Until the publication of the report of the WHO Scientific Group on the Measurement of the Public Health Importance of Bilharziasis in 1967 (17), clinical descriptions of schistosomiasis were largely restricted to hospital and clinic observations on individuals; the more recent population-based epidemiological studies have provided a new perspective on the spectrum of clinical disease and on the evolution of disease in untreated as well as treated persons. The use of new techniques such as ultrasound and isotope renography offers unique possibilities to measure morbidity in hospitals as well as in the communities of endemic areas.
Control programmes that adopt a strategy of morbidity reduction will integrate measurements of disease at the various levels of operation. These programmes should collaborate with the sectors of the health delivery system, such as university hospital pathology and clinical services, outpatient facilities, etc., that will provide data to monitor the impact of the programme on the population at risk.

A standardized classification is required for the accurate monitoring of infection and morbidity over time, so that comparisons can be made between countries. The present Expert Committee reviewed the sections of the International Classification of Diseases, Ninth Revision (18) that relate to schistosomiasis, its complications, and sequelae (Table 2), and recommended major changes (see section 7.2, recommendation 13).

The early stages of infection with the three major schistosome species that affect man are similar; differences are apparent when the infection is well established and different systems in the host are involved. A description of the course of schistosomiasis was prepared by a WHO Scientific Group convened in 1965 (17) and is still considered to be valid (Table 3).

2.1 *Schistosoma mansoni*

Because of the comparative ease with which this parasite can be maintained in the laboratory it has been used more often in experimental infections in animals than other schistosome species. In addition, since the main sequelae of human infection—liver and spleen enlargement—can be detected without the use of invasive methods of investigation, community-based studies of morbidity can be carried out more readily than for *S. haematobium* infections.

2.1.1 Pathology

Post-mortem studies involving worm recovery and the assessment of tissue egg densities have confirmed the relationship between morbidity and the intensity of infection. Other genetic factors such as ABO blood groups and certain antigens of the HLA system may determine the intensity of infection, although this has not been confirmed in all studies.

Although the overall pathological picture is unchanged, an analysis of the pattern of post-mortem data in Brazil suggests that
Table 2. Extract from the *International Classification of Diseases*, ninth revision

### A. Underlying infection

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>Schistosomiasis [bilharziasis]</td>
</tr>
<tr>
<td>120.0</td>
<td><em>Schistosoma haematobium</em></td>
</tr>
<tr>
<td>120.1</td>
<td>Vesical schistosomiasis</td>
</tr>
<tr>
<td>120.2</td>
<td><em>Schistosoma mansoni</em></td>
</tr>
<tr>
<td>120.3</td>
<td>Intestinal schistosomiasis</td>
</tr>
<tr>
<td>120.4</td>
<td>Asiatic schistosomiasis, Katayama disease or fever</td>
</tr>
<tr>
<td>120.8</td>
<td>Cutaneous</td>
</tr>
<tr>
<td></td>
<td>Cercarial dermatitis, Schistosome dermatitis</td>
</tr>
<tr>
<td></td>
<td>Infection by cercariae of <em>Schistosoma</em></td>
</tr>
<tr>
<td></td>
<td>Other*</td>
</tr>
<tr>
<td></td>
<td>Infection by <em>Schistosoma intercalatum</em></td>
</tr>
<tr>
<td></td>
<td>Infection by <em>Schistosoma mattheei</em></td>
</tr>
<tr>
<td>139</td>
<td>Late effects of other infectious and parasitic diseases</td>
</tr>
</tbody>
</table>

### B. Manifestation in organ system*

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>153</td>
<td>Malignant neoplasm of colon*</td>
</tr>
<tr>
<td>154</td>
<td>Malignant neoplasm of rectum, rectosigmoid junction and anus*</td>
</tr>
<tr>
<td>155</td>
<td>Malignant neoplasm of liver and intrahepatic bile ducts*</td>
</tr>
<tr>
<td>188</td>
<td>Malignant neoplasm of bladder*</td>
</tr>
<tr>
<td>344</td>
<td>Other paralytic syndromes</td>
</tr>
<tr>
<td>345</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>416.9</td>
<td>Pulmonary heart disease, unspecified, cor pulmonale (chronic)</td>
</tr>
<tr>
<td>456.0</td>
<td>Oesophageal varices with bleeding</td>
</tr>
<tr>
<td>456.1</td>
<td>Oesophageal varices without mention of bleeding</td>
</tr>
<tr>
<td>456.2</td>
<td>Oesophageal varices in cirrhosis of liver</td>
</tr>
<tr>
<td></td>
<td>(M8210/0) 596 Adenomatous polyp</td>
</tr>
<tr>
<td>571.5</td>
<td>Cirrhosis of liver without mention of alcohol</td>
</tr>
<tr>
<td>572.3</td>
<td>Portal hypertension</td>
</tr>
<tr>
<td>581</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>583.8</td>
<td>Nephritis and nephropathy not specified as acute or chronic—With other specified pathological lesion in kidney</td>
</tr>
<tr>
<td>591</td>
<td>Hydronephrosis</td>
</tr>
<tr>
<td>592</td>
<td>Calculus of kidney and ureter</td>
</tr>
<tr>
<td>594</td>
<td>Calculus of lower urinary tract</td>
</tr>
<tr>
<td>599.7</td>
<td>Haematuria</td>
</tr>
<tr>
<td>786.1</td>
<td>Dysuria</td>
</tr>
<tr>
<td>786.2</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>789.2</td>
<td>Splenomegaly</td>
</tr>
<tr>
<td>791.0</td>
<td>Proteinuria</td>
</tr>
</tbody>
</table>

*Infections by *Schistosoma bovis* and *Schistosoma spindale* probably do not occur in man.

*See section 7.2 recommendation 13 for proposed changes.

*Use code for morphology of neoplasms if feasible and indicate underlying infection.

Changes are occurring which are thought to be due to the widespread use of antischistosomal drugs, among other factors, during the past 10 years. The overall number of persons found to have hepatic and splenic enlargement on autopsy is progressively decreasing; the cases occurring in young patients are becoming rare, and there appear to be more cases in which death in advanced schistosomiasis seems to be due to other major and unrelated diseases. In one university
<table>
<thead>
<tr>
<th>Stage of disease</th>
<th>Parasitological characteristics</th>
<th>Clinical characteristics</th>
<th>Pathological characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Invasion</td>
<td>(a) Penetration</td>
<td>Cercarial skin reaction, if present</td>
<td>Papular dermatitis</td>
</tr>
<tr>
<td></td>
<td>(b) Migration</td>
<td>Fever, cough, if present</td>
<td>Inflammatory reactions in lungs and liver</td>
</tr>
<tr>
<td>(2) Maturation</td>
<td>Completion of maturation and early oviposition, with migration to definitive sites</td>
<td>Acute febrile illness, not always recognized or present</td>
<td>Hyperergic reactions, generalized and local, to products of eggs and/or young schistosomes (experimental animals)</td>
</tr>
<tr>
<td>(3) Established infection</td>
<td>Intensive oviposition, accompanied by a corresponding excretion of eggs</td>
<td>Stage of early chronic disease, characterized, for instance, by haematuria or intestinal and other digestive manifestations</td>
<td>Focal inflammatory reactions due to eggs, resulting mainly in granulomas; fibrosis is not a predominant feature</td>
</tr>
<tr>
<td>(4) Late infection and complications</td>
<td>Prolonged infection often with reduced or discontinued excretion of eggs</td>
<td>Stage of discrete syndromes such as in portal hypertension, cor pulmonale, fistula, obstructive uropathy, and renal failure; serological findings are indicative of presumptive diagnosis</td>
<td>Vascular and fibrotic lesions of variable degree</td>
</tr>
</tbody>
</table>

*Modified from Table 1 in the report of the WHO Scientific Group on the Measurement of the Public Health Importance of Bilharziasis (17).

Pathology service in north-east Brazil between 1956 and 1976, hepatosplenomegaly due to *S. mansoni* infection was found in 6.7% of autopsy cases; between 1976 and 1980 this figure fell steadily to 1.9% and the deaths were mostly among an older age group than previously. Similar data are not available from other endemic countries where antischistosomal drugs have been widely used.

2.1.2 Clinical manifestations

Community-based studies have drawn attention to the few symptoms that are associated with the majority of *S. mansoni* infections, but in some areas the frequency of the symptoms that occur is related to the intensity of infection. Weakness and lassitude are rarely associated with the infection, diarrhoea is associated with
only very high levels of egg excretion, but abdominal pain and blood in the stools, both overt and as detected by chemical reagents, tend to increase with the intensity of infection.

(1) Hepatic and splenic enlargement. In four community-based studies in Africa, South America, and the Caribbean, hepatomegaly and splenomegaly were found to be more common in individuals with a heavy infection. The most common relationship found in these studies suggests that one would be unlikely to find hepatomegaly and hepatosplenomegaly among 5–14-year-olds in areas with a low intensity of infection, which is usually associated with a low prevalence. The availability of standardized methods would enable more reliable comparisons to be made and the use of ultrasound might obviate problems arising from different criteria of hepatomegaly and observer variation. The liver receives most of the eggs that are retained in the body. As a result, liver enlargement, predominantly of the left lobe, is the most common manifestation of *S. mansoni* infection in most endemic areas. Liver function is usually normal and the enlarged firm liver may be the only abnormality. The most frequent consequence of hepatosplenic disease is haematemesis, which may occur without warning; it may cause early death, or repeated episodes may occur. When hepatosplenomegaly develops before puberty, retardation of growth and infantilism have been observed.

(2) Pulmonary hypertension and cor pulmonale in hepatosplenic disease. After the development of portal hypertension with collateral circulation, *S. mansoni* eggs may be diverted into the pulmonary circulation system and may obstruct small blood vessels. Individuals with hepatosplenomegaly due to *S. mansoni* infection may have cyanosis and clubbing in the absence of, or with only mild, pulmonary hypertension. It is a matter of debate whether this is caused by pulmonary arteriovenous fistulae or portopulmonary anastomoses.

(3) Colonic polyposis. Hepatosplenicomegaly due to *S. mansoni* infection in Egypt and East Africa appears to be similar to that reported from Brazil, but the most important difference in the development of sequelae is the occurrence of rectocolonic polyps in Egypt. In one survey these polyps were found in 12% of persons with hepatosplenomegaly and were associated with the production of bloody diarrhoea which may cause marked anaemia and hypoproteinaemia.
(4) Renal involvement. Proteinuria has been found in 12–15% of patients with hepatosplenomegaly. All types of glomerular lesions have been found in heavy and long-standing infections, although chronic membranous proliferative glomerulonephritis predomi-
nates. IgG and IgM complexes and schistosomal antigens have been found in basement membranes and in mesangial areas.

(5) Tumoral lesions. Occasionally large pseudoneoplastic masses may develop that are rich in calcified eggs, granulomas, and fibrous tissue. They are found in the descending colon, sigmoid, and epiploon.

(6) Central nervous system. Eggs, although larger than capillaries, may be carried along and deposited in the lungs and the central nervous system by passing through pathologically altered pulmonary vessels, perhaps arteriovenous anastomoses or from the primary sites via the vertebral venous system. Rarely, adult worms are found in the central nervous system, producing local depositions of large numbers of eggs and resulting in the development of serious lesions.

When myelopathy occurs, myelograms may be normal or reveal an irregular, partial, or complete myelographic block. Radiculitis of the cauda equina has also been reported. These conditions usually respond to antischistosomal drugs.

More cases of involvement of the central nervous system are reported from South America and the Caribbean than from Africa but even so such involvement is rare, although it may occur more frequently than is generally appreciated. Post-mortem studies in a number of countries have reported the presence of schistosome eggs in the central nervous system. In contrast to the lesions due to S. japonicum infection, those due to S. mansoni infection usually involve the spinal cord rather than the brain.

2.1.3 Effect of treatment on disease

The acute phase of infection may be treated successfully with the currently available antischistosomal drugs after egg excretion is initiated.

Late-stage, severe forms of the disease observed in Brazil and Egypt have also been treated safely. In Brazil, compensated hepatosplenic disease has been shown to respond well to treatment, with a marked reduction in liver and spleen size in 50% of patients and in some cases complete regression has occurred within about six
months. Decompensated hepatosplenic disease may also be treated safely, but any improvement in these patients is due more to hospital care and diet than to therapy alone.

Specific treatment and supportive care of patients with pulmonary schistosomiasis can result in an improvement in the symptoms of those with relatively low-grade pulmonary hypertension, but not in patients with cyanosis.

Patients with diffuse colonic polyposis respond well to specific treatment. In 90% of subjects, parasitological cure is accompanied by a significant reduction in polyp size, with complete regression occurring in some patients; this size reduction is accompanied by increases in haemoglobin, serum albumin, and serum iron.

Some acute cases of spinal cord involvement showing an intramedullary mass and urine retention, and apparently due to *S. mansoni* infection, resolve rapidly and completely after treatment and it is suggested that immediate treatment of such cases may obviate the need for surgical intervention.

### 2.2 Schistosoma haematobium

In the past twenty years, clinical and pathological studies have established the public health importance of *S. haematobium* infection. It has been shown that: (a) there is a relationship between intensity of infection and severity of disease including the probability of sequelae/complications; (b) the disease progresses from active to inactive stages; (c) the deposition accumulation of eggs is focal; and (d) these factors are related to morbidity and mortality.

#### 2.2.1 Pathology

While *S. haematobium* worms are widely distributed throughout the pelvic and mesenteric venous plexuses, oviposition takes place mainly in the pelvic organs, especially the lower urinary tract and distal gut. Infections with *S. haematobium* appear to be intermediate between *S. mansoni* and *S. japonicum* infections, both quantitatively and qualitatively. *S. haematobium* infection produces granulomas with multiple eggs, which frequently calcify.

#### 2.2.1.1 Intensity of infection. In post-mortem studies the intensity of infection has been assessed directly by quantifying the worm burden, and indirectly by determining the egg burden in the tissues.
Both the eggs and the disease persist after the adult worms have disappeared, while a significant proportion of deposited eggs calcify and are subsequently retained in the tissues; approximately 90–100 eggs per female worm per day accumulate in the tissues.

2.2.1.2 Progression of the disease. Active urinary schistosomiasis is characterized by the presence of viable adult worm pairs, oviposition, and a vigorous granulomatous response. The excretion of ova in the urine occurs in proportion to the number of viable eggs in the tissues and in the lower urinary tract, and the number of worms present, not in proportion to the tissue egg burden or intensity of previous infection. The number of calcified eggs in the tissue progressively increases during active disease. This stage of the disease is epidemiologically important because of its role in transmission and clinically important because obstructive sequelae can usually be improved at this stage with chemotherapy.

Inactive urinary schistosomiasis is characterized by the absence of adult worms and viable eggs in the tissues or urine. If there is urinary excretion of dead or calcified eggs then the number found is not proportional to the tissue egg burden and this excretion most frequently occurs as a result of complications (schistosomal ulceration or urothelial malignancy). If the number of calcified eggs in the tissues exceeds 20 000–30 000 eggs per gram of tissue then they can be detected radiologically. Severe schistosomal disease may persist and become clinically symptomatic even when eggs are no longer found in the urine. Epidemiological studies based on urinary egg excretion show that the prevalence of urinary schistosomiasis is lower in persons aged 30 years or more; however, autopsy studies do not confirm this observation because the proportion of inactive cases increases in this age group.

2.2.1.3 Disease in different organs.

(1) Urinary bladder. Schistosomal disease of the bladder includes polyposis, ulceration, urothelial hyperplasia, metaplasia and dysplasia, and urothelial malignancy. Histological grading of the severity of disease is positively correlated with the tissue egg burden of the bladder.

(2) Ureters and schistosomal obstructive uropathy. Schistosomal obstructive uropathy (hydroureter and hydronephrosis) is the most frequent and serious sequela of urinary schistosomiasis. Three
autopsy studies have established with certainty that both conditions are related to the intensity of infection (i.e., tissue egg density). Patients with schistosomal hydroureter and hydronephrosis were found to have higher tissue egg counts than those with hydroureter alone. Patients with bilateral disease were found to have higher tissue egg burdens than those with unilateral disease. Obstructive uropathy was found to be correlated, in descending order, with the egg concentration in the upper ureters, interstitial ureters, lower ureters, and the bladder.

(3) Urinolithiasis. Ureteritis cystica calcinosa is associated with severe infection with S. haematobium, but is not associated with pyelonephritis. In Egypt, ureterolithiasis, but not nephrolithiasis, was more common in S. haematobium infections than in uninfected controls and was associated with pyelonephritis and urinolithiasis.

(4) Gastrointestinal tract involvement. Tissue egg density progressively increases towards the distal intestine, especially from the splenic flexure and sigmoid colon. The density in the appendix is generally higher than in adjacent regions of the gut. Appendicitis may become symptomatic during heavy infections, and mortality directly due to active schistosomiasis is associated with (not caused by) a very high egg density in the appendix.

2.2.1.4 Unusual ectopic lesions. Ectopic migration of S. haematobium worms and oviposition can occur anywhere in the body. Central nervous system involvement is well documented, the spinal cord being affected more often than the brain.

2.2.2 Clinical manifestations

Clinical manifestations in the early stages of invasion and maturation are rarely seen in the indigenous population of endemic areas and most patients are unaware that they are infected. Once the infection is established, haematuria is the first and commonest clinical sign; it may be accompanied by dysuria and an increased frequency of micturition (in the absence of a bacterial infection), particularly in well established cases. Vague abdominal pain is common but clinical examination is usually negative.

Schistosomal hydronephrosis develops with progressive renal pelvic dilation, medullary atrophy, and then cortical atrophy, which correlates with the clinical observation that tubular function,
especially concentration, is compromised before glomerular function decreases and, in part, explains the remarkable recovery of renal function after treatment. Hydroureter usually precedes hydronephrosis; thus, hydronephrosis represents an advanced stage in the succession of sequelae. Both hydroureter and hydronephrosis occur less frequently on the left side of the urinary tract.

Reports from Africa have demonstrated the extent of severe urinary tract disease within apparently healthy communities in endemic countries. Typical findings among infected persons are hydronephrosis, deformed ureters, and calcified bladders (the latter may be a risk factor associated with bladder cancer—see section 2.4). In several studies the frequency of urinary tract pathology in children has been shown to be related to the intensity of infection as assessed by quantitative egg excretion; however, further community-based studies relating the intensity of infection to urinary tract pathology (possibly using ultrasound) are required to define this relationship more clearly.

An excess of lesions has been observed in male adults older than 20 years when compared with the 5–19-years age group. The lesions do not occur with the same frequency among females although the prevalence and intensity of infection are similar in the two sexes.

Although haematuria is present, severe anaemia is not associated with the infection. The levels of leukocyturia, proteinuria, and haematuria are related to the intensity of infection. Mild hypertension has been associated with *S. haematobium* infection in South Africa but not in East Africa, the Gambia, or Nigeria. Bacteriuria has been associated with *S. haematobium* infection in hospitalized patients in Egypt and also in a field study in the Gambia, but not in other areas. The pus cells frequently reported to be present in urine are probably mostly eosinophils derived from the inflammatory lesions formed around the eggs in the bladder wall.

1. *Pyelonephritis and other kidney diseases.* There is a marked increase in the occurrence of pyelonephritis in patients with severe schistosomal obstructive uropathy. Taking all the clinical and autopsy data into consideration it seems probable that the presence of schistosomal obstructive uropathy, urolithiasis, bladder outlet obstruction, and bacterial cystitis all predispose to pyelonephritis. No consistent association has been shown in man between *S. haematobium* infection and glomerulopathy, hypertensive nephropathy, or amyloidosis.
(2) Sterility and infertility. Schistosomiasis, particularly infection with *S. haematobium* may involve any part of the genital tract. The reported prevalence and distribution of schistosomal lesions in the various genital organs vary markedly in different studies. The severity and functional effects of the lesion including infertility, ectopic pregnancy, and miscarriage, depend on its size and site.

Among women, the cervix and the vagina are most commonly affected. Viable *Schistosoma* ova may be recovered from cervical mucus and can be detected in 2–7% of routine cervical smears in different endemic areas. Massive granuloma may, however, occur in any part of the genital tract and papillomatous growths on the vulva and vaginal wall have been reported. The tissue egg density is greatest in the vaginal wall and cervix, less in the ovaries and fallopian tubes, and still less in the other parts of the genital tract.

At least two well-designed studies with appropriate controls have failed to demonstrate a relationship between the presence of schistosome eggs in the fallopian tubes and the occurrence of ectopic pregnancies.

Among men, the involvement of the seminal vesicles, prostate, and testicles has been reported on several occasions, but no association with impotence and sterility has been demonstrated.

2.2.3 Effect of treatment on disease

- After treatment, the symptoms disappear and there is a reduction in egg excretion, proteinuria, haematuria, urinary iron loss, and leukocyturia. Among children radiological abnormalities tend to regress following treatment, but among adults they tend to persist and may even progress in some cases. Both praziquantel and metrifonate have been shown to reduce the frequency and intensity of proteinuria and haematuria, particularly in children.

Studies in Africa show that the majority of obstructive uropathy abnormalities due to large granulomas in children may be reversible with treatment and may even be spontaneously reversible. In other studies in Egypt involving older persons (mean age 21.5 years), conventional urography showed no improvement in obstructive lesions following treatment despite the reversal of renogram and renal function test elevations. There is evidence that calcification of the bladder may be reduced by treatment but further investigation is required.
Improvements in anthropometric indices have been reported in schoolchildren following treatment.

2.2.4 *Schistosoma intercalatum*

There are no reports describing the pathology of *S. intercalatum* infection in man. The clinical manifestations are similar to those of *S. mansoni* infection and its sequelae. The use of the drug praziquantel is highly effective against *S. intercalatum* infection. The effect of treatment on morbidity due to *S. intercalatum* infection has not yet been evaluated.

2.3 *Schistosoma japonicum* and Asian schistosomes that infect man

Disease due to *S. japonicum* has been recognized in man and animals since the last century, but a related parasite, *S. mekongi*, has been identified only within the past 20 years; it causes a disease similar to that due to *S. japonicum*. More recently a related zoonotic parasite has been found in Peninsular Malaysia.

2.3.1 Pathology

As for other schistosome infections, the primary lesion following infection with *S. japonicum* is a granulomatous reaction to the egg. The immune response responsible for the formation of the granuloma of *S. japonicum* may be different from that causing the granuloma around *S. mansoni* or *S. haematobium* eggs. T lymphocytes are of major importance in the formation of granulomas around both *S. mansoni* and *S. japonicum* eggs, but the modulation of the size of the granulomas is primarily cell-mediated for *S. mansoni* and antibody-mediated for *S. japonicum*. Part of the granuloma formation associated with *S. japonicum* infection appears to require neither antibody nor T lymphocytes. In spite of these differences in the regulation of tissue reactions, the principal pathological lesion of the liver produced by the two species, i.e., periportal fibrosis, is similar.

In comparison with *S. mansoni* and *S. haematobium* infections less information exists on the pathology of *S. japonicum* infection in man. Apart from the "pipe-stem" periportal fibrosis which is also characteristic of *S. mansoni* infection, extensive intralobular fibrosis may be present. A general correlation has been observed between the
presence and severity of fibrosis and the number of eggs recovered
from digested tissues. In the intestines the number of eggs recovered
increases from the small bowel to the rectosigmoid region and
predominates in the submucosa. Compared with *S. mansoni*
infection, the gastrointestinal tract lesions tend to be focal, isolated,
and of a more proliferative type.

*S. japonicum* eggs, like those of *S. haematobium*, frequently calcify
in the tissue, where they may accumulate since they are not efficiently
removed by the host. The pathogenic significance of the presence of
calcified eggs is unknown, but they are generally surrounded by only
a slight cellular reaction.

Cirrhosis, as opposed to periportal fibrosis of the liver, is
sometimes attributed to *S. japonicum* infection, but there are no data
to support the hypothesis that the cirrhosis observed in man is
caused by the schistosome infection rather than being coincidental
to it.

The pathology in man of infection with *S. mekongi*, a close
relative of *S. japonicum*, has not been described.

2.3.2 Clinical manifestations

Infection due to *S. japonicum* causes a spectrum of clinical disease
similar to that observed for *S. mansoni* infection. Historically a more
severe clinical picture is ascribed to *S. japonicum* infection. The
difference is attributed to a higher egg output from *S. japonicum* and
to the fact that its eggs are laid in large aggregates that stimulate a
more intense tissue reaction. Population-based epidemiological
studies in the Philippines have indicated that morbidity due to
*S. japonicum* is similar to that due to *S. mansoni* in persons with
comparable faecal egg counts. Further epidemiological studies using
comparable quantitative techniques should be carried out.

Acute schistosomiasis appears to have been most frequently
described in individuals who had not been previously exposed or
resided in an endemic area.

The early chronic stages of disease, as in *S. mansoni* infection, are
manifested generally by anaemia, diarrhoea, dysentery, and
abdominal pain; the severity of these symptoms depending on the
intensity of infection determined in population-based studies. The
clinical measurement of liver size, particularly of the left lobe below
the xiphoid, has been recognized as useful by field workers and has
been used as an index of the prevalence of schistosomiasis in the
national control efforts in Japan since the 1930s. More recently, population-based epidemiological studies have shown that there is a correlation between the intensity of infection and liver enlargement in all age groups. The most severe liver disease due to *S. japonicum* infection occurs in persons between 20 and 40 years of age. Severe portal hypertension may be associated with the shunting of eggs into the pulmonary circulation, causing cor pulmonale. The frequency of this clinical condition depends on the intensity of infection in a population, but data from population-based studies are unavailable and this problem will require further investigation. Hepatic coma, as a terminal event in liver disease due to *S. japonicum* infection, has been observed in hospitalized patients, particularly in China. In the Philippines the most frequent terminal event is massive haematemesis.

Involvement of the central nervous system in *S. japonicum* infection occurs in about 1 person per 1000 infected individuals. In the Philippines the most frequent clinical manifestations observed were Jacksonian seizures and psychomotor seizures, the onset of which occurred after 21 years of age. Among individuals with seizure activity as the first symptom, 20% later developed hemi- or monoparesis with or without motor aphasia. Caution must be exercised in diagnosing cerebral involvement and the simultaneous presence of other parasitic infections or other diseases must be considered.

### 2.3.3 Effect of treatment on disease

Praziquantel is well tolerated by patients with severe forms of clinical disease. In long-term follow-up studies carried out four years after a single treatment with praziquantel, both hepatomegaly (in 73% of cases) and splenomegaly (in 94% of cases) were found to have regressed to normal. These clinical improvements were accompanied by a reduced level of specific antibody as determined by the ELISA and circumoval precipitation tests. Following treatment in man, immunological parameters, including the levels of immunoglobulin and specific IgG and IgM, as well as lymphocyte blast transformation rates all decrease to be within normal ranges.
2.3.4 *Schistosoma mekongi*

In the floating villages of Democratic Kampuchea the peak prevalence of *S. mekongi* infection occurs in children below 10 years of age. The early phases of infection are similar to those observed following *S. japonicum* infection. Hepatomegaly, particularly enlargement of the left lobe of the liver, has been observed in 50% of those infected, predominantly in school-age children. Splenomegaly has been observed in about one-third of persons with hepatomegaly.

Clinicians have commented on the apparent high rate of clinical portal hypertension and have suggested that the clinical manifestations of *S. mekongi* infection may be more severe than those of *S. japonicum* infection.

*S. mekongi* infection responds well to praziquantel. An increase in the white blood cell count and the number of eosinophils has been observed immediately after treatment. Liver size regresses to normal within 7–10 months after treatment.

2.3.5 A species of *Schistosoma* found in Malaysia

The first nine cases of schistosomiasis from Peninsular Malaysia were identified from autopsies made on Orang Asli (aborigines), but schistosome eggs have never been found in stool samples, either from an individual who had eggs in a liver biopsy specimen or from others with a positive circumoval precipitation test (using eggs from the Malaysian schistosome species). Little information is available on the clinical manifestations of this infection in man and this parasite is presumed to cause a zoonotic infection.

2.4 Carcinoma and schistosomiasis

Trematodes are among the organisms most frequently associated with an elevated risk of developing a neoplasm. The role of schistosomiasis in the etiology of cancer is controversial. Advanced *S. mansoni* infection has been associated with follicular lymphoma of the spleen, but not with colorectal cancer, hepatoma, or bile duct carcinoma. *S. japonicum* infection has been linked with hepatoma and colorectal cancer and *S. intercalatum* infection with experimentally induced bladder cancer. However, most of the
information available involves *S. haematobium* infection which has been associated with a number of malignancies, most notably bladder cancer.

The relationship between infection with *S. haematobium* and bladder cancer was reviewed by the present Expert Committee. There are several lines of evidence suggesting that such an infection can be a major cause of bladder cancer in a number of countries:

1. **Comparative case-control studies:** in endemic areas a higher rate of *S. haematobium* infection is generally found in individuals with bladder cancer than in controls; and a higher rate in cases of squamous cell bladder cancer than in other histological types of bladder cancer.

2. **Primary site of bladder cancers:** the trigone of the bladder is rarely the primary site of cancer in cases associated with *S. haematobium* infection. Calcification of the bladder due to *S. haematobium* infection appears to be a risk factor associated with squamous cell bladder cancer.

3. **Geographical correlation:** there is a positive correlation between the number of cases of bladder cancer and *S. haematobium* infection rates in Africa.

The mechanisms by which *S. haematobium* infection may predispose to carcinoma of the bladder have not yet been established. Some suggestions include: (a) the carcinogenic effects of nitrosamines produced as byproducts of secondary bacterial infections; (b) synergism between tobacco smoking and schistosomiasis; and (c) the carcinogenic effects of abnormal tryptophan metabolites resulting from normal hepatocellular function in patients with severe disease and coexistent *S. mansoni* infection.

*S. japonicum* infection was implicated as a cocarcinogen in carcinoma of the rectum and carcinoma of the liver before the lifetime of the parasite had been described. Granulomatous disease of the rectum and sigmoid colon with mucosal hyperplasia pseudopolyposis, ulceration, thickening of the bowel wall, and stenosis may occur. The mean age of *S. japonicum* infected individuals with carcinoma of the colon or rectum was found to be 10 years less than that of uninfected individuals. The rate of carcinoma of the colon in one series of autopsies was 25 times greater in infected persons than in uninfected persons. The carcinoma of the colon associated with *S. japonicum* infection has been characterized.
as a well-differentiated adenocarcinoma with pseudopolyps and calcified eggs usually present in the tissues.

An association between hepatoma and *S. japonicum* infection has not been confirmed. In one autopsy series in Japan the rate of hepatoma in infected individuals was about four times that found in uninfected individuals.

2.5 Other conditions associated with schistosomiasis

2.5.1 Bacteraemia due to Gram-negative bacteria

Bacteraemia due to *Salmonella* spp. has been associated with all schistosome species affecting man. Blood cultures are frequently positive and bacteria can sometimes be found in faeces and urine. The bacteria are localized on the surface or in the intestinal tract of adult worms. These infections are characterized by periods of prolonged fever and respond to antischistosomal therapy. Antibiotic treatment for *Salmonella* alone is not effective.

In *S. mansoni* infections more than 20 species of *Salmonella* of human and animal origin have been isolated from patients with hepatosplenic disease; *Escherichia coli* has also been isolated from blood cultures although *in vitro* worm culture reveals no adherence of these bacteria to the surface of the worm. *S. japonicum* and *S. intercalatum* infections have been associated with *Salmonella typhi* and *Salmonella paratyphi*. *Salmonella enteritidis* has also been associated with *S. intercalatum* infection. *S. haematobium* infection has been associated with *Salmonella typhi*, *Salmonella paratyphi* A, B, and C, and *Salmonella dublin*.

2.5.2 Hepatitis B virus

In hospital-based studies of patients with *S. mansoni* infection, hepatosplenic patients have an increased prevalence of hepatitis B surface antigen (HBsAg) and such infections may be associated with the more severe form of decompensated liver disease. In contrast, there is no evidence of an association between *S. japonicum* infection and the presence of hepatitis B virus in community or post-mortem studies.
2.5.3 Nutrition and schistosomiasis

While the majority of people with schistosomiasis are undernourished, any of the three major species of schistosomes can per se increase nutrient losses from the body through blood and protein loss in the urine or protein and electrolyte loss in diarrhoea.

Among children with heavy *S. haematobium* infections, height, weight, skin-fold thickness, and haemoglobin levels have been observed to be lower than in uninfected children or those with lesser infections. Significant improvements in growth and haemoglobin level occur after treatment. Urinary iron losses in infected children returned to normal levels after treatment and any decreased physical fitness is rapidly reversed.

*S. mansoni* infection causes blood loss in the stool, but the magnitude of this loss over time in infected persons and its significance for their nutritional status, remains unclear. Heavily infected persons have been shown to have lower haemoglobin levels than those with lesser infections. The effect of massive protein loss, associated with intestinal polyposis due to *S. mansoni* infection, on the nutritional status is unknown.

2.6 The immune response to schistosomiasis in man

The immune response to *Schistosoma* infection in man is not fully understood. Within programmes designed to control morbidity primarily through the use of chemotherapy, evidence concerning the development of immunity, the risk of developing disease, and the development and maintenance of resistance to reinfection should be investigated in close collaboration with research institutions. Continued support for research related to the immune response to schistosomiasis in man is desirable.

2.6.1 Humoral immune response

Despite the existence of a large body of literature on immunodiagnostic tests for schistosomiasis in man, none of the available techniques has been satisfactorily applied to the control of schistosomiasis.

In the individual patient, when purified antigens are used, the isotypic antibody responses to specific antigens can be correlated with relevant clinical conditions such as duration and intensity of
infection and even some states of modulated responsiveness. A marked IgG response as well as an IgM response to a proteoglycan antigen from the gut of the schistosome has been observed in many acutely infected patients.

High IgE levels are associated with many parasitic infections as well as with allergic states. Specific IgE levels are generally low in persons with acute Schistosoma infection, but may become elevated at later stages of infection.

The level of circulating immune complexes appears to be higher in acute schistosomiasis than in chronic infection without severe sequelae. Circulating immune complex levels are high in persons with severe hepatic and splenic enlargement.

2.6.2 Associations between disease and immunity

Epidemiological data indicate that persons infected with Schistosoma parasites develop some form of immunity to subsequent reinfection. The characteristics of this immunity may be more fully examined in endemic areas where antischistosomal drugs are being used. In many control programmes and pilot epidemiological research projects it has been consistently observed that the prevalence and intensity of infection are reduced rapidly and that this reduction is sustained for up to two years or more. As yet, no in vitro effector immune mechanism has been identified that correlates with this apparent resistance to reinfection. Furthermore the in vivo effector mechanisms have not yet been explored.

Some studies indicate that the in vitro immune regulatory mechanisms are abnormal in persons with severe disease or in those who are heavily infected and that these abnormalities disappear after successful treatment.

3. METHODS OF CONTROL

New drugs and diagnostic techniques, together with other technical advances, have radically improved the possibilities of controlling morbidity. The beneficial effect of these methods of control, when used in conjunction with those for transmission control, is now widely recognized. Within the aims of health for all by the year 2000 and also those of the International Drinking Water Supply and Sanitation Decade there is renewed appreciation that the
maintenance of schistosomiasis morbidity control can be undertaken through primary health care. While chemotherapy, improved environmental management, and snail control can all contribute to the eventual control of schistosomiasis, the human host—the vector of the parasite—can probably contribute most to the long-term solution of the problem following sustained and appropriate health education, distribution of health information, and community participation.

3.1 Health education

Efforts should be made to modify knowledge, attitudes, and perceptions with respect to the transmission, diagnosis, and control of the disease. Since behaviour is often determined by local culture, it may not be easy for control programmes to achieve appropriate behavioural changes within a short time. Health education and communication should not be the responsibility of the professional health educator alone, but should involve all members of the control team, and, in particular, be community based. A health education programme will be more likely to succeed if it is designed for the particular community in question, if it encourages the community to initiate and accept responsibility for parts of the programme, and if it emphasizes positive rather than negative aspects. The communication techniques used should be simple, inexpensive, and of a technical level that can be maintained and/or produced by the members of the community. Educational programmes must remain flexible so that they can be changed as the control programme evolves. Above all, health education must be recognized as being an important and integral part of the control programme by both the technical and managerial staff.

3.1.1 Behaviour, morbidity, and recognition of symptoms

Since behavioural change can reduce the risk of infection, and a willingness to cooperate in a treatment regimen is crucial to the success of chemotherapy, health education can significantly contribute to a strategy to reduce morbidity.

Daily water-contact behaviour as well as the type of water supply available are of fundamental epidemiological importance. A beneficial modification in behaviour would be, for example, to change the time for bathing, irrigating, or collecting domestic water
to early morning when the cercarial count is low. When clean water supplies and sanitation are introduced, it will be necessary for the population to modify their behaviour and use these in preference to traditional sources of water. An inability to modify behaviour is often due to a disregard for social mores or to inadequate explanation of the use and advantages of the modern installations. Water collection and the washing of clothes at a river bank provide an opportunity for women and their children to gather and it is important that safe alternative water supplies should maintain this tradition.

Ignorance and fear are not the only impediments to successful diagnosis and treatment. The economic costs of treatment (the price of the drug, the working days lost because of attendance at clinics, etc.) may discourage a patient from seeking help until morbidity is far advanced. Health education should stress the advantages of early as well as preventive action.

3.1.2 Health for all by the year 2000

3.1.2.1 Community participation. Community participation is regarded as an essential element of any schistosomiasis control programme, whether this involves the community installing its own water supply or simply cooperating with the health authorities to reduce contact with unsafe sources of water. The rationale of community participation lies in the reduction of costs and the assurance that longer-term intervention measures (such as environmental improvements) will be maintained after the withdrawal of the control team.

Health education in this context will involve discussions with community members so that culturally acceptable responses to health problems can be found. It is important to recognize that communities are not homogeneous units, and that the provision of health facilities is likely to be used in local power struggles. Knowledge of the social structure of the community is a prerequisite if community participation is to be achieved.

The full participation of women in the health education process is particularly important. Their potential role in promoting the health of their families and their influence in helping to prevent schistosomiasis in their children should be stressed in the health education activities carried out in the community.
3.1.2.2 Approaches for community participation. Since schistosomiasis is essentially a “man-made” disease, community involvement is an essential element in any schistosomiasis control programme. Each community is a separate cultural entity and the approach taken to ensure maximum community involvement must take into account this fact, which has been all too often ignored in the past.

3.2 Diagnostic techniques

Simple, rapid, and economical quantitative techniques are now available for urine and stool examination. The results obtained using these techniques are highly consistent between technicians, so that valid comparisons can be made between endemic areas. Such data can be analysed statistically and in this way quality control, a critical aspect of any control programme, is made easier.

The consideration of prevalence data alone will not be enough to determine whether transmission control has been achieved. An analysis of the data on the intensity of infection is a more precise epidemiological indicator of the extent of morbidity as well as of the level of transmission. The quantitative data derived from these diagnostic techniques are an indirect measure of the morbidity related to Schistosoma infection. Data of this type are important in the evaluation of the effectiveness of a schistosomiasis control programme whose objective is the reduction of morbidity.

3.2.1 Stool examination techniques

The cellophane faecal thick-smear technique (Kato) using a standardized template to measure a defined amount of faeces (ranging from 10 to 50 mg) is recommended for the diagnosis of S. mansoni, S. japonicum, and S. intercalatum infections. Considerable experience with this technique in national control programmes in Brazil and Burundi has confirmed its usefulness. Accurate egg counts are obtained 30 minutes after preparation of the slides and a qualitative result to identify infected persons needing treatment can be obtained immediately.

In some endemic areas the intensity of infection may be usually below 100 eggs per gram of faeces either naturally or because of the activities of a control programme. In such areas the sensitivity of a single Kato slide is inadequate to detect all infected persons. In these
areas several Kato slides should be prepared to increase the sensitivity of the test or a more elaborate method should be used such as the quantitative modified Ritchie formol-ether concentration technique.

3.2.1.1 Egg count categories for stool examinations. The quantitative data from stool examinations for the detection of *S. mansoni*, *S. japonicum*, *S. mekongi*, or *S. intercalatum* eggs may be reported according to egg count categories. These categories are derived from population-based epidemiological studies that assess the relationship between intensity of infection and morbidity, i.e., liver and spleen size. In children, liver and spleen enlargement are both correlated with the intensity of infection. Most epidemiological studies agree that the correlation becomes statistically significant at 100 or more *S. mansoni* or *S. japonicum* eggs per gram of faeces. As an example, the egg counts obtained by the cellophane faecal thick-smear technique using the Kato-Katz template (41.7 mg of faeces) may be reported in the following categories:

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>No. of eggs per Kato-Katz slide</th>
<th>Range of number of eggs per gram of faeces</th>
<th>Rate of hepatomegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light</td>
<td>1–4</td>
<td>24–96</td>
<td>Rare</td>
</tr>
<tr>
<td>Moderate</td>
<td>5–33</td>
<td>120–792</td>
<td>Frequent</td>
</tr>
<tr>
<td>Heavy</td>
<td>≥ 34</td>
<td>&gt;816</td>
<td>Almost always</td>
</tr>
</tbody>
</table>

If few heavy infections are present, the use of intermediate categories may be appropriate.

3.2.2 Urine examination techniques

Filtration techniques are rapidly replacing qualitative sedimentation techniques for the analysis of urine. For diagnosing *S. haematobium* infection, syringe filtration of a random 10-ml aliquot of urine using Nytrel (nylon), Nuclepore (polycarbonate) or paper filters is recommended. These filters are held in a Swinnex-type filter support usually of 13-mm diameter; for research purposes a 25-mm diameter support may be used.

3.2.2.1 Egg count categories for urine examinations. The quantitative data obtained from urine examinations using the syringe filtration technique for the detection of *S. haematobium* infection may be reported according to egg count categories.
Population-based epidemiological and clinical studies have been used to assess the relationship between proteinuria or haematuria and *S. haematobium* infection. In the majority of these studies a high proportion of children excreting more than 50 eggs per 10 ml of urine are found to have haematuria and/or proteinuria as detected by chemical reagent strips. Limited experience is available on the use of the following categories and modification may be required to include a third, higher egg count category:

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>No. of eggs per 10 ml of urine</th>
<th>Haematuria in children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light</td>
<td>1–49</td>
<td>Frequent</td>
</tr>
<tr>
<td>Heavy</td>
<td>&gt; 50</td>
<td>Almost always present</td>
</tr>
</tbody>
</table>

Two additional reasons for selecting 50 eggs per 10 ml of urine as an upper limit for urinary egg counts are: (a) the lack of reproducibility of higher counts between microscopists or by the same microscopist; and (b) the length of time taken to count more than 50 eggs. A third category such as > 500 or > 1000 *S. haematobium* eggs per 10 ml of urine may be appropriate in areas where the intensity of infection frequently (> 10%) reaches this level.

3.2.3 *Indirect diagnostic techniques*

Diagnostic chemical reagent strips that measure semiquantitative levels of urinary blood or protein are commercially available. The reagent strips have been evaluated for both sensitivity and specificity and have been compared with quantitative parasitological techniques in different age groups. In general, about 80% of all infected children and about 98–100% of those with more than 50 eggs per 100 ml of urine have haematuria that is detected by reagent strips. Among adults the proportion of infected persons with haematuria is lower. Because of the epidemiological differences it is suggested that indirect diagnostic techniques be evaluated and compared with quantitative parasitological techniques before they are recommended for widespread use.

3.2.4 *Miracidial hatching techniques*

These are highly sensitive techniques for the detection of *Schistosoma* infections and in clinical trials of antischistosomal drugs they are essential to determine the viability of *Schistosoma*
eggs. However, these techniques have not been well standardized and further improvements are needed since they may be useful in evaluating control programmes, particularly in the later stages of the programme when the prevalences and intensities of infection are low.

3.2.5 Immunodiagnostic techniques

The role of the available immunodiagnostic techniques is to be viewed in comparison with the simple, low-cost, quantitative parasitological techniques in use in national control programmes. Research in this area is being actively pursued by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. A collaborative study on the antigens for immunodiagnosis of schistosomiasis, jointly supported by that programme and the Edna McConnell Clark Foundation (13), indicated that no available antigen or test system is better than current parasitological techniques for identifying active infection. This evaluation indicated that immunodiagnostic tests for *S. japonicum* infections using homologous antigens, particularly those of egg origin should be developed further in anticipation of their future usefulness.

While overt human infections with animal schistosomes are infrequently reported, there is some evidence that they may cause false positive results in immunodiagnostic tests.

3.3 Chemotherapy

The primary objective of chemotherapy in schistosomiasis control should be the reduction and prevention of morbidity (4).

Whenever antischistosomal drugs are to be used: (a) the objectives to be achieved by the use of chemotherapy must be clearly defined; (b) it is important to choose the most appropriate drugs; (c) the correct dosage schedule must be followed; and (d) adequate information on the drug and its side-effects must be widely available in the health delivery system.

High cure rates are achieved following treatment with all the new antischistosomal drugs. Even if egg excretion persists after treatment, the intensity of infection is greatly reduced, and the risk of developing disease among those who were previously heavily infected is greatly reduced.
Although there is great interest in the antischistosomal drugs, there is also concern about their cost for large-scale use. The cost can be reduced if the drugs are obtained by direct, bulk purchase through the national schistosomiasis control programmes or as part of a national drug policy (see section 5.4.5).

Of the many drugs that display antischistosomal activity, only three can be considered for large-scale chemotherapy: metrifonate, oxamniquine, and praziquantel. The current antischistosomal drugs (Table 4) are listed in the full WHO model list of essential drugs (20, p. 20), but not in the reduced model list of 22 drugs for primary health care (20, p. 40–41; see also section 5.3.4).

Table 4. Properties of antischistosomal drugs included in the WHO model list of essential drugs

<table>
<thead>
<tr>
<th>Property</th>
<th>Type of schistosomiasis</th>
<th>Mefronate</th>
<th>Oxamniquine</th>
<th>Praziquantel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic efficacy estimated cure rates</td>
<td>S. mansoni</td>
<td>Negligible curative effect</td>
<td>60% to over 90%</td>
<td>60–90%</td>
</tr>
<tr>
<td>S. haematobium</td>
<td></td>
<td>40% to over 80%</td>
<td>Ineffective</td>
<td>80–95%</td>
</tr>
<tr>
<td>S. japonicum</td>
<td></td>
<td>Negligible curative effect</td>
<td>Ineffective</td>
<td>60–80%</td>
</tr>
<tr>
<td>Estimated population acceptance of the standard dose*</td>
<td>S. mansoni</td>
<td>Not applicable</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>Estimated population tolerance*</td>
<td>S. haematobium</td>
<td>Good</td>
<td>Not applicable</td>
<td>Good</td>
</tr>
<tr>
<td>S. japonicum</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>Mode of administration</td>
<td>3 doses, each of 7.5–10 mg/kg, at 2-week intervals</td>
<td>In South America, the Caribbean, and West Africa, a single dose (15 mg/kg adults; 20 mg/kg children). In Africa, treatment over two days usually necessary; 30–60 mg/kg total dose</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Varies markedly with age.
3.3.1 Metrifonate

Metrifonate, formerly known also as trichlorophone and trichlorofone, is an organophosphorus ester that is active only against S. haematobium. The drug is rapidly absorbed, metabolized, and excreted. Two metabolic pathways have been identified, both giving rise to DDVP (2,2-dichlorovinyl dimethyl phosphate) a cholinesterase inhibitor that acts directly; this is the active compound and metrifonate acts as a slow-release formulation.

The pharmacology of metrifonate has been studied extensively in many experimental animal models. No undue pathophysiological effects other than its anticholinesterase activity have been found at dose levels comparable to those used in man. The mode of action of metrifonate in schistosomiasis remains unknown.

Extensive toxicological studies have demonstrated a wide margin of safety for metrifonate. No mutagenic activity has been established. Carcinogenicity studies in four mammalian species were negative. Embryotoxicity and teratogenicity have not been found in laboratory tests. In spite of these negative findings, administration of the drug during pregnancy is not recommended.

The standard drug regimen is 7.5-10 mg of drug per kg body weight given in 3 doses at 2-week intervals. Other suggested regimens using single 10-mg/kg doses at intervals of 3, 6, or 12 months have not been evaluated sufficiently in the field to be recommended; research is in progress to determine their efficacy.

(1) Side-effects. Tolerance of the drug is good. Cholinergic side-effects are rare, generally mild, and disappear within a few hours. Thus, metrifonate may be considered to be an example of a drug that inhibits cholinesterase, but whose potentially harmful side-effects do not occur at therapeutic dose levels.

If severe cholinergic symptoms occur, 1.0 ml of atropine sulfate should be given parenterally once, or repeatedly if necessary. The undesirable side-effects will be diminished but the antiparasitic efficacy will not be reduced. Pralidoxime iodide is an enzyme reactivator for use in cases of life-threatening enzyme inhibition. There are no reports that this enzyme reactivator has had to be used following the administration of metrifonate in over a million treatments given so far.

Occupational groups recently exposed to organophosphate insecticides should be treated with metrifonate only when a
pretreatment determination of blood cholinesterase shows the level to be normal. If such determinations cannot be done or cholinesterase levels are lower than normal, it is preferable to postpone treatment or to use another antischistosomal drug.

(2) Therapeutic index. The cure rates in schistosomiasis control programmes range from 40 to more than 80%, with a 90% reduction in egg counts among individuals who are not cured. In one group of clinical trials, the cure rate at 6 months among persons who received 1 dose of metrifonate was 28%, among those receiving 2 doses, 65%, and after 3 doses, 84%.

3.3.2 Oxamniquine

Oxamniquine is a tetrahydroquinoline that is active only against S. mansoni infection. The adult male S. mansoni worms are more susceptible to oxamniquine than the female worms. Although the precise mode of action is not known, worm death has been observed to be associated with the formation of large subtegumental vesicles. The early developmental stages of S. mansoni are also vulnerable to oxamniquine.

There are distinct differences in the response to drug therapy of schistosome strains of South American and African origin. In South America, the Caribbean islands, and West Africa, a single dose of 15 mg of oxamniquine per kg is adequate for adult patients. Infections in children are less responsive than those in adults, and it is recommended that patients under 14 years of age in South America and the Caribbean are treated with a single total dose of 20 mg/kg or with 2 doses of 10 mg/kg in one day separated by 3–8 hours. In Africa, the efficacy of the drug was determined largely in children, and no distinction is made there between the recommended doses. In East and Central Africa (Kenya, Madagascar, Malawi, Rwanda/Burundi, United Republic of Tanzania, Zambia) and the Arabian peninsular, a total dose of 30 mg/kg, given as 15 mg/kg twice in one day or on consecutive days, is required. This dose is increased to 40 mg/kg in Sudan, Uganda, and Zaire. S. mansoni infections in Egypt, South Africa, and Zimbabwe need to be treated with a total dose of 60 mg/kg, administered as 15 mg/kg twice daily for 2 days or 20 mg/kg as a single dose for 3 consecutive days. Ethiopia occupies an intermediate position, both geographically and in terms of dosage, between East Africa and Egypt.
(1) *Side-effects.* Oxamniquine is well tolerated, especially if given after a meal. The most frequent side-effects observed have been dizziness, drowsiness, and headaches. These side-effects occur 1–2 hours after ingestion and rarely last more than 6 hours. Vomiting and diarrhoea are infrequent. Hallucinations, psychic excitement, and epileptiform convulsions following the administration of oxamniquine have been reported rarely. Post-treatment fever has been observed in the 24–72 hours following treatment. In practice these side-effects have not limited the use of the drug in large-scale treatment programmes. Patients with a known history of epilepsy should be treated with caution and under supervision, and concomitant prophylaxis with an anticonvulsant should be considered.

(2) *Therapeutic index.* After treatment, the appropriate therapeutic dose of oxamniquine can be expected to produce a cure rate of at least 60%, and often more than 90%. Among patients who are not cured, egg excretion will be reduced by over 80% and usually by over 90% one year after treatment. Oxamniquine has been used widely for the treatment of rural communities on both an experimental and a routine basis, with several million treatments having been administered by paramedical personnel operating in local health centres or as mobile teams.

3.3.3 *Praziquantel*

Praziquantel is a heterocyclic pyrazino-isoquinoline that is effective against *Schistosoma mansoni*, *S. haematobium*, *S. japonicum*, *S. mekongi*, *S. intercalatum*, and *S. mattheei* (1). Efficacy is limited neither by the geographical origin of the parasite species or subspecies, nor by age, sex, kind, or origin of the many strains of host animal. Its efficacy has also been established against liver, lung, and intestinal flukes as well as all human cestodes.

Special attention has been paid to testing this drug for mutagenicity. Comprehensive toxicological studies employing a wide variety of test systems have been carried out by WHO in collaboration with the International Agency for Research on Cancer. No mutagenic, carcinogenic, embryotoxic, or teratogenic activity of praziquantel has been established.

Although considerable research has been carried out to elucidate the mechanism of action of praziquantel, it cannot yet be explained
at the molecular level, but it is known to be associated with strong muscular contraction and tegumental vesicle formation.

A single dose of praziquantel of 40 mg/kg is recommended for *S. haematobium* or *S. intercalatum* infections. The same or a slightly higher dose, up to 60 mg/kg, may be required in certain areas for *S. mansoni* or mixed infections. For *S. japonicum* infections, the present recommended regimen is 2 doses of 30 mg/kg (total dose 60 mg/kg) given with a 4-hour interval.

(1) **Side-effects.** Praziquantel is well tolerated. The main side-effects are abdominal discomfort, diarrhoea, dizziness, and sleepiness.

Fever and skin rash have been reported more infrequently. All side-effects are less frequent when the treatment is for a *S. haematobium* infection. Advanced hepatosplenic schistosomiasis has been successfully treated with praziquantel without any adverse side-effects.

For the treatment of *S. japonicum* infections, side-effects including fainting, hallucinations, psychotic symptoms, and excitement have been observed for up to 15 days after medication. The very rapid elimination of the compound from the human body suggests that these effects are unlikely to be due to the drug. The relationship between these clinical manifestations and cerebral infection due to *S. japonicum* has not been fully evaluated.

(2) **Therapeutic index.** The cure rate for *S. haematobium* infection in the field is usually between 80 and 95%. The reduction in egg count in those who are not cured is usually 90–95% one year after treatment. A lower cure rate has been observed in combined *S. mansoni* and *S. haematobium* infections. Cure rates for *S. mansoni, S. intercalatum, S. japonicum,* and *S. mekongi* infections have been generally reported to be more than 60% after one year with a 95% or greater reduction in egg count in those who are not cured. To date, approximately 1 million persons have been treated with praziquantel.

3.3.4 **Combination drugs**

In some endemic areas combinations of drugs have undergone trials (especially for *S. haematobium* infection) in order to
circumvent drug delivery problems, i.e., multiple doses, or to attempt to reduce costs.

The use of combinations of drugs is acceptable only when each single ingredient is essential and when the combination provides a clear and significant therapeutic advantage over the constituent drugs given separately. The scientific proof of superior therapeutic efficacy in man usually demands rigorous protocols and field trials. Results reported in the literature are rarely firm enough to withstand statistical or clinical pharmacological criticisms. It is the responsibility of the manufacturers of drug combinations to ensure, as far as is technically possible, that toxicity in man is not enhanced by the combination and that incompatibilities are unlikely to occur.

3.3.5 Drugs under development

3.3.5.1 Amoscanate. At least 6 different formulations of this isothiocyanate anthelmintic have been administered to human volunteers, including patients with hookworm infection and others infected with one of the three principal schistosome species or with *Wuchereria bancrofti*. Two small-particle-size formulations (<2 µm) of amoscanate are equally effective in rodents against the three main species of *Schistosoma* infecting man. These oily and aqueous suspensions show considerably enhanced antischistosomal activity compared with the micronized (particles 1 µm in diameter) active substance of the tablets used for clinical trials. At present, the first of two formulations is undergoing double-blind, phase-I clinical trials in volunteers.

In China, hundreds of thousands of patients with *S. japonicum* infection were treated with nithiocyaninum (this drug has been synthesized and developed in China, and is the same as amoscanate). Some 2000 cases treated with four different formulations are documented in the literature. All these cases received the drug repeatedly during 3–7 days in dosage forms of suboptimal particle size (3–6 µm in diameter). Complaints of side-effects (dizziness, dreaming, anorexia, abdominal pain, etc.) were reported in up to 80% of patients. It is not clear whether a dose-relationship was observed. The incidence of jaundice (6.6% after a total dose of 7 mg/kg given in 3 daily doses) appeared to be related to both the formulation and the total dose of the drug. Jaundice tended to
occur 4–19 days after the end of treatment and resolved after about 1 week.

3.3.5.2 Ro 13-3978. Since the previous Expert Committee (19), the clinical development of Ro 11-0761 and Ro 11-3128 has been terminated owing to poor tolerance by man. Ro 13-3978 is an effective oral schistosomicidal agent in experimental infections of mice, hamsters, and monkeys. This substance has shown marked curative activity against Schistosoma mansoni, S. haematobium, and S. japonicum. Laboratory testing is continuing.

3.3.6 Resistance to drugs

Because of experience with other parasitic diseases, and the large-scale use of new antischistosomal drugs, the possibility of drug resistance occurring has been recognized. This drug resistance might be used to differentiate subspecies.

Resistance to oxamniquine and bcyanthone can be induced experimentally and is genetically transmitted, the resistance being maximal in the F1 generation. There is side-resistance between oxamniquine and bcyanthone, possibly because the drugs may have a similar mode of action in inhibiting parasite nucleic acid synthesis, but S. mansoni infections that fail to respond to oxamniquine may respond to praziquantel. In Brazil, strains of S. mansoni have been isolated from patients whose infection has not been completely cured by repeated standard doses of oxamniquine or bcyanthone. Although inherent parasite susceptibilities differ, there is no evidence that there will be a rapid appearance of complete resistance that will render the drug useless, nor is there any justification for restricting the use of oxamniquine, or any other effective antischistosomal drug, in community treatment. All the resistant S. mansoni strains are susceptible to praziquantel.

3.4 Snail control

The three methods of snail control—chemical, environmental, and biological—have been used in the past to control snail hosts and have been comprehensively reviewed in recent years.

During the past decade numerous control projects in Brazil, Congo, Egypt, Ghana, Jordan, Madagascar, Philippines, United Republic of Tanzania, Venezuela, Zimbabwe, and elsewhere have
shown that snail control by molluscicides, in combination with other methods, can reduce or eliminate transmission. There is, however, a major need for the development of new synthetic molluscicides to increase the impact of the other advances made in schistosomiasis control. Snail control procedures, including mollusciciding, will therefore remain among the methods of choice for the control of schistosomiasis, even though selective population-based chemotherapy now plays the leading role in integrated control strategies.

3.4.1 Available molluscicides

Available molluscicides must be safe—i.e., non-toxic for mammals and other aquatic organisms; they must not produce unacceptable adverse effects if they enter the food chain; and they must be stable in storage. Other considerations include cost and availability, snail specificity, low toxicity for non-target species, acceptable formulations, simple means of application, and a reliable method of field analysis.

(1) Niclosamide. At present this is the molluscicide of choice (2); it is marketed under the name of Bayulscide. A similar chemical product is known in Egypt as Mollutox.

(2) Copper. Copper salts have been largely discarded by most snail control programmes since their mollusccidal efficacy, irrespective of method of application (in slow-release matrices, in chemical barriers, in compounds of different anionic nature, etc.) has been less than satisfactory. Moreover, the cost-effectiveness of the use of copper sulfate, despite its low purchase price, has been shown to be unacceptably high in comparison with that of niclosamide.

3.4.2 Molluscicides under development

(1) Organotins. The high molluscicidal activity of a number of organotin compounds is well known. The molluscicidal activity appears to be limited to the trisubstituted molecules, as has been demonstrated against Bulinus spp., Biomphalaria spp., and certain operculate freshwater molluscs. The organotins have not proved to be very effective against the amphibious oncomelaniid snails. Certain organotin compounds have been incorporated into slow-release rubber formulations that permit low dosing rates to be achieved for long periods. However, insufficient information is at
present available to assess the long-term toxicity to man and his domestic animals. Such information is at present being recorded on bis(tri-n-butyltin) oxide (TBTO), a potentially effective molluscicide. A review of the toxicology, pharmacology, and other relevant aspects of the organotins has recently been published (6).

(2) Amide compounds. The action of fluoracetamide and its analogues (bromoacetamide, chloracetamide) against amphibious and aquatic snails has been investigated. The toxicological effects on man and the environmental impact of these compounds have not been assessed. These compounds have high molluscicidal activity and low toxicity to fish, and are water-soluble, stable, and easy to apply. The results of small-scale field trials indicate that they are particularly suitable for use in fish ponds.

(3) Molluscicides of plant origin. The most promising plant molluscicides at present available are certain strains of Phytolacca dodecandra (endod), and Jatropha curcas from the Philippines. However, they each have their limitations. No plant molluscicide is specific to snails, and few have been adequately tested under simulated field conditions. Long-term toxicological studies have not, as yet, been undertaken on any vegetable molluscicide, and the same toxicological regulations apply to these compounds as apply to synthetic products. The role of plant molluscicides has recently been extensively reviewed and discussed (11). Further research in this area can be expected.

3.4.3 Toxicity, mutagenicity, and carcinogenicity testing

Almost all candidate molluscicides have undergone adequate short- and medium-term (90 days) toxicity testing, but few have been subjected to long-term toxicological studies. Niclosamide is the only molluscicide that has undergone carcinogenicity testing.

3.4.4 Resistance to molluscicides

Observations suggesting that the snail intermediate hosts of Schistosoma can develop resistance to molluscicides will require further study. Increased tolerance to niclosamide has been reported among Bulinus truncatus from an area in the Islamic Republic of Iran. Bulinus truncatus from trifenmorph-treated areas of the Gezira
in Sudan were found to be 1.2–1.3 times less susceptible to this molluscicide (which is no longer in use). After five successive generations, Biomphalaria glabrata reared in the laboratory and subsequently exposed to copper sulfate and niclosamide have shown an approximately two-fold higher tolerance to both molluscicides. However, in the field, no evidence of resistance of B. glabrata to either copper sulfate or niclosamide has been reported. Studies have been inconclusive with respect to the resistance of Oncomelania spp. to sodium pentachlorophenate.

There is still no firm evidence that snail hosts can develop levels of resistance to molluscicides that are high enough to affect snail control operations.

3.4.5 Laboratory screening of molluscicides

In 1965, the World Health Organization published guidelines for the screening and evaluation of molluscicides (16). The methods and recommendations established at that time remain valid today. In 1971, WHO established criteria for preliminary, definitive, and comprehensive laboratory screening procedures for molluscicides against both aquatic and amphibious snail hosts.1

Two laboratories, one in Japan for amphibious snails and the other in the United States of America for aquatic snail hosts, have been designated as WHO Collaborating Centres for studies on molluscicides.

3.4.6 The market for molluscicides

Paradoxically those countries that most need molluscicides are often those that are least likely to be able to afford them. Consequently, the market available for existing or new molluscicides is limited. The development costs of a new synthetic molluscicide from initial laboratory trials to market availability have been estimated to be approximately 10 million US dollars. It is not surprising, therefore, that no new molluscicide has become available since before the previous Expert Committee meeting (19).

---

3.4.7 Mollusciciding costs

Data on the cost-effectiveness of chemical snail control operations are few and comparisons of costs between one endemic area and another may be unrealistic. Figures of 1–4 US$ per capita annually have been reported, and the cost-effectiveness of mollusciciding is greatest where the volume of water to be treated per person at risk is small. Molluscicides are particularly well suited to relatively arid areas where transmission sites are relatively small and seasonal. Mollusciciding may also be cost-effective in large, flowing, or static waterbodies now that it is recognized that schistosomiasis transmission tends to be focal rather than widespread. Even in some large irrigation schemes, where human population density is high and where water-management mechanisms are sophisticated, area-wide mollusciciding can be cost-effective.

3.4.8 Future role of molluscicides in schistosomiasis control

Population-based chemotherapy combined with health education and focal and seasonal mollusciciding are likely to be the most important features of schistosomiasis control operations in high-priority endemic foci. The application of molluscicides must be carefully planned to take advantage of focal and seasonal patterns of transmission; it also requires efficient management, well-trained and motivated staff, and sufficient funds for supplies and activities. Better strategies and delivery systems will be needed to improve the cost-effectiveness of mollusciciding. In particular, there is a great need, at present, to develop new, low-cost, effective synthetic molluscicides to add to the single compound that is commercially available.

3.4.9 Biological control

Recently interest has been focused on competitive interaction between snails, and several potential competitor-snails have been identified. The most promising candidates appear to be Thiara granifera, Marisa cornuarietis, Biomphalaria straminea, and Helisoma duryi. The last-named snail has been found to prefer an ecological niche different from that of the target species, and the pilot studies involving this species have not been successful. That competition can actually occur and cause the displacement of a host snail has been observed in Martinique, where B. straminea appears
to have naturally replaced *Biomphalaria glabrata*. However, *B. straminea* is a host of *S. mansoni* in Brazil and its use as a competitor snail is not recommended, at present. Recent studies in St Lucia suggest that *T. granifera* can replace the host snail *B. glabrata*, but these findings will require further investigation.

3.5 Environmental management and modification

3.5.1 Irrigation schemes

Water-resource projects are essential components of the development process in many endemic countries. Measures to reduce snail populations and hence the risk of transmission of schistosomiasis or to prevent its spread, are not usually considered during the planning of such projects. The costs of altering designs may be high, e.g., overhead sprinkler systems instead of canals and provision for adequate periodic drainage of small reservoirs or irrigation systems, but there may be a long-term economic benefit. Planners and engineers involved in water-resource development projects should be informed of possible design and management practices that will minimize any adverse effects on public health.

In some areas, overhead sprinkler and trickle irrigation systems are being used increasingly to improve water management and to reduce water usage and waste through evaporation. These methods also assist schistosomiasis control by reducing the number of open canals and drains and hence direct human contact with water. In areas where open canal irrigation systems still operate, two important and low-cost management practices outlined below may contribute to reducing intermediate snail host populations.

(a) Periodic removal of vegetation from the irrigation canals will reduce the size of the intermediate snail host population since it forms their primary shelter. Periodic alteration of the water level in the irrigation canals, particularly complete drainage, not only reduces the amount of aquatic vegetation but also strands and kills the snail host by dessication.

(b) The lining of canals with either rubber or cement is often necessary to prevent seepage or silting. It also limits the growth of vegetation and therefore reduces the vector population and schistosomiasis transmission. Modification of canal design to improve water flow may also reduce snail populations. The inclusion
of night storage tanks in the design of irrigation schemes should be avoided.

During the planning of irrigation schemes there should be strict control of the siting of human settlements; these should be well away from canals and should be provided with properly maintained and adequate water supplies and sanitary facilities. Public standpipes should be provided with proper facilities to allow the waste water to drain away effectively so that new snail habitats are not created.

3.5.2 Natural habitats

Often, around villages there are water bodies (e.g., borrow pits) that may be transmission sites and therefore should be filled. Marshy areas can be filled or drained and used for development purposes. Rivers, particularly near towns, can be canalized to make the edges unsuitable for snails. Alternatively, all obstructions (including weeds) that affect water flow and cause still “backwaters” that might harbour snails should be removed.

The presence of aquatic vegetation is extremely important in many habitats. Since snails frequently aestivate around roots when sites dry out, it may be advantageous to clear the vegetation, including roots. This applies particularly to small water-holes that are frequently transmission sites, and also to dry irrigation canals.

3.5.3 Man-made reservoirs

Various attempts have been made to alter the physical environment in such a way as to induce changes in the transmission potential of schistosomiasis. Weed clearance is one means and the well-documented WHO/UNDP Lake Volta project serves as a good example. Another attempt to create lacustrine conditions that did not favour transmission was carried out on Lake McIwaine in Zimbabwe between 1972 and 1975.

The environmental management of fish ponds, which are usually ideal snail habitats and important sites of transmission, has been neglected. Fish ponds should be constructed so that they can be drained periodically and so that contact between man and the water is limited; in addition, adequate sanitary facilities should be provided in the vicinity. Road construction in endemic areas may create new sites of transmission because of poor drainage and excavation.
3.5.4 Environmental modification

All unnecessary water bodies should be removed by filling-in or drainage and, wherever possible, obvious water-contact sites should be made less accessible to users. For example, where fording is common, a bridge should be built and, where a site is particularly popular as a children's play place, then either an alternative (such as a cheap swimming pool) should be constructed or the dangerous site should be fenced off.

3.6 Sanitation and water supply

The aim of these measures is to reduce the contamination of water habitats and to reduce human contact with water; both approaches must be accompanied by intensive health education and should be provided as part of community participation in primary health care. If these aims are achieved the impact on schistosomiasis control is likely to be more permanent than the improvements obtained using the short-term, disease-specific control measures of chemotherapy and snail control. In addition, other socioeconomic benefits can be expected.

3.6.1 Sanitation

The widespread use of improved latrines would, in the long term, have an effect on transmission, although in the short term this is unlikely.

The construction and use of suitable and acceptable latrines should be encouraged to improve the general standard of hygiene and to reduce canal contamination, post-excretion water contact, and also the incidence of other faecal-borne diseases. The ventilated pit latrines used in Zimbabwe (fly-proof and free of odour) are a major improvement on the usual pit latrine extensively used in developing countries. Furthermore, because they can also serve as washrooms, their provision may have an additional effect on schistosomiasis transmission since an acceptable bathing facility near the home offers an attractive alternative to the stream. The appropriate design of sanitation facilities has recently been
comprehensively reviewed by the World Bank/UNDP global project for low cost sanitation technology.¹

3.6.2 Water supply

Water-contact studies in many endemic areas show a remarkable similarity in the pattern of contact with water for domestic purposes. The collection of water for home use, washing clothes, household utensils, bathing, and playing makes up a large proportion of observed contacts with water in many cultures. These contacts mostly involve children and women and their number can be greatly reduced by the provision of adequate, safe water that is available at more convenient sites than the infected sources and in systems that are properly maintained.

Rural water supplies vary considerably between and within different endemic areas. Commonly, a few public standpipes are provided to supply “safe” potable water. These may be adequate for some domestic needs but in St Lucia and Zimbabwe this form of water supply has not been found to prevent water contact for washing clothes, bathing, and play, all of which involve either exposure of small areas of the body for prolonged periods, or extensive bodily exposure for short or long periods and which are therefore all associated with a high risk of schistosome infection. When a public standpipe system of water supply was supplemented by laundry facilities and showers in St Lucia a marked reduction in water contact was observed. In Zimbabwe, after the installation of simple concrete washing slabs, there was a 50% reduction in river contacts for washing clothes. In the consolidation phase of control in St Lucia, no resurgence of transmission occurred during a 4-year follow-up study following selective population chemotherapy in villages with a public standpipe water supply supplemented with laundry and shower units. In villages where no supplementary units were provided, the prevalence increased.

Improved water supply systems are not necessarily expensive to install. In Zimbabwe, protected water supplies using drilled tubewells and a simple bucket pump system cost less than 5.00 Zimbabwe dollars per person, and in some areas 2.00 Zimbabwe dollars per person.

¹ World Bank/United Nations Development Programme. Development and implementation of low cost sanitation investment projects. Interregional Project INT/80/047, Transportation and Water Department, World Bank, Washington DC, USA.
dollars per person for the materials, with labour recruited locally and at no cost. Approximately 20 litres of water are consumed per person per day in Zimbabwe; consumption has been estimated to be 15 litres in St Lucia.

3.7 Data management

At all stages, a schistosomiasis control programme requires quantitative information on the different aspects of operations. However, a single index such as prevalence of schistosomiasis within a defined population is not sufficient for the purposes of monitoring or modifying the operations of a control programme. Other indices are needed, especially those relating to the reduction in morbidity.

Modern statistical methods facilitate, to a large extent and on an objective basis, the interpretation of data in which variations may be due to the simultaneous action of many factors. For this reason, statistical methods should be used at all phases of a schistosomiasis control programme, in the establishment of the operational plans as well as in the monitoring of the operations and the final evaluation of the results.

3.7.1 Requirements for data analysis in the control of schistosomiasis

In general, much more data are accumulated by a control programme than can be analysed correctly or used satisfactorily. Rational planning should be flexible, adapted to local conditions, and practicable within the limitations of available funds and trained personnel to analyse the data.

The geographical area to be covered, the timing of the observations, the methods and frequency of intervention, and reasonable targets for achievement, should be rationally established. This requires definitions to be established and standardized classifications to be used. Questionnaires and record forms appropriate for use in the data-collection procedures must be pre-tested. It is most important that the staff responsible for data collection are suitably trained; the procedures for their supervision and quality control should be established.

Where examination of the total population is not feasible, statistical methods should be used to select appropriate sampling schemes. The evaluation of the campaign results, the assessment of
the statistical significance of the conclusions, and the timely preparation of reports on the progress of the programme, and particularly their dissemination to field workers, are important activities of the statistical services.

The analysis and interpretation of the data should not be entirely the responsibility of a central statistical service. Each operational level of the programme should be capable of making specific judgements concerning the efficiency of the operations within its sector and should only pass to the next level essential information for further analysis.

3.7.2 Sources of the information necessary for the preparation and implementation of control

(1) Demographic statistics. In general, a population census should be carried out at the beginning of the programme. Each locality should be defined by careful mapping and the population size determined by a household census. Where a census is not feasible, the best estimate that can be obtained through discussions with local officials or community leaders may be used. This estimate should also give some indication of the distribution of the population by age, migration, and growth rate.

(2) Parasitological findings. In order to monitor and evaluate a schistosomiasis control programme properly it is necessary to calculate certain indices both before and during the programme. The most appropriate indices (see Annex 1) are based on quantitative measurements made on the population.

(3) Morbidity due to schistosomiasis. In most countries the public health services have established a system for the obligatory notification of certain infectious diseases, in particular those considered to be highly contagious and dangerous. Unfortunately, statistics concerning the treatment of cases in hospitals and health centres are often the only sources of information on the prevalence of schistosomiasis. These data must be interpreted with caution.

Since the aims of control programmes are now directed towards a reduction in morbidity due to schistosomiasis, it is necessary that more up-to-date and reliable information is obtained on morbidity both at the beginning and during a control programme. Indices related to morbidity are given in Annex 1.

(4) Chemotherapy of schistosomiasis. During a control programme, other indices based on the treatment of the population
may be calculated. Programmes dealing with individuals on a community basis rather than in hospitals, etc., will require some new terminology or redefinition of terms. For example, it is proposed that the word “cure” is replaced in control programmes by the term “egg negative”, this term being defined as the absence of Schistosoma eggs in a treated individual. Indices related to chemotherapy are given in Annex 1.

(5) Other assessment indices. Although the examination of the population is essential for the evaluation of the programme, changes in other biological and sociological indicators should also be taken into consideration, e.g., reduction in the snail population; reduced contact with water; reduced cercarial levels at the water-contact sites; and introduction or increase of water supply systems and sanitation facilities.

3.8 Training

Persons responsible for national training should have an in-depth knowledge of the control methods, investigational techniques, and epidemiology of schistosomiasis. Those trained should be prepared not only to perform their particular tasks, but also to train other staff in the health delivery system.

Major changes are taking place in the training activities of successful public health programmes of all types. The technology used in these training schemes is being critically evaluated in each country to determine whether it is appropriate for the programme in that particular country. It is being increasingly recognized that a thorough training in epidemiology and vector biology is needed in order to be able to develop rational operational approaches and to assess achievement. The reorganization of the managerial process and infrastructure to improve the efficiency of operations is another important sign of progress in national control programmes. Since the targets of morbidity control can be rapidly achieved, it is necessary that there is a general awareness of the importance of schistosomiasis control principles at all levels of the health delivery system.

The implementation of a strategy for morbidity control instead of transmission control or eradication requires a fundamental change in approach. This strategy must concentrate on specific quantitative goals and immediate changes in approach must be made as soon as these goals are reached.
In-service training of the personnel involved in a national schistosomiasis control programme is an important form of supervision. Periodic in-service training programmes can be used to inform the staff of advances or changes in technology and methodology, review the standard operational procedures, and evaluate the implementation and progress of the control activities.

Regional training activities should be encouraged. The technical cooperation between endemic countries is increasingly important as they realize that different strategies are required for morbidity control in different situations. Exchange of personnel between countries involved in schistosomiasis control would facilitate the transfer of knowledge and even of successful techniques.

The WHO Parasitic Diseases Programme has developed a 5-day training programme for the supervisory staff of schistosomiasis control programmes and for the staff of the general public health services. Since 1982 this course has been successfully evaluated in Egypt, Morocco, St Lucia, and Zimbabwe and repeated by national staff in several programmes. The time-frame is flexible and may be adapted to local or regional needs. This approach to training emphasizes actual field experience using the techniques and methodology recommended for control programmes. The Committee highly commends this training programme and approves its continued use.

4. REVIEW OF PROGRESS IN NATIONAL PROGRAMMES

4.1 Countries where *S. mansoni* is endemic

4.1.1 Brazil

The Special Programme for Schistosomiasis Control was initiated in 1976 in eight states in north-east Brazil. The population at risk was estimated to be more than 5 600 000 persons. The aim of the programme was to eliminate transmission and to reduce prevalence to less than 4%.

The approach to control included the treatment of the entire infected population with oxamnique, the periodic application of molluscicides in epidemiologically important transmission sites, health education, and an improvement in sanitation and water supplies.

70
Stool examinations were performed for all schoolchildren aged 7–14 years, using the cellophane faecal thick-smear technique (Kato-Katz). The population to be treated by chemotherapy was determined using the findings of the school surveys:

(a) where prevalence was greater than 20%, the whole population of the municipality was treated without further examination (mass treatment);

(b) where prevalence was between 4% and 20%, treatment was given to all those between 5 and 25 years of age (selected group therapy);

(c) where prevalence was below 4%, only infected children were treated.

Chemotherapy was used throughout the endemic area and other methods of control were applied when feasible. Initially schoolchildren were re-examined at 6-month intervals. Later in the programme this re-examination was carried out at 12-month intervals. Repeat treatments were given on the basis of the criteria used for the initial treatment.

The operational guidelines were modified several times during the programme. Evaluation of the programme has not yet been completed. The prevalence rates are now less than 4% in the states of Ceará and Rio Grande do Norte (12.2 and 20.7%, respectively, before control). In the states of Paraíba and Sergipe the prevalence is now less than 10%. In the states of Pernambuco and Alagoas the prevalence has been reduced by about 50%. In the state of Sergipe during the past 7 years, there has been a marked decrease in hospital admissions of patients with hepatosplenomegaly due to *S. mansoni* infection.

During the first 6 years of this programme, the cellophane faecal thick-smear technique (Kato-Katz) was used as a qualitative parasitological technique to determine the prevalence among school-age children. Since 1982 the objective of the programme has been to control morbidity, rather than to control transmission, and to avoid the spread of the disease to new areas. Quantitative egg counts are now reported and progress is being assessed by the reduction in intensity of infection as well as by changes in prevalence. Reduction in prevalence as well as in intensity of infection after population-based chemotherapy has been maintained for longer periods than was anticipated. Now, annual re-examinations and treatment (rather
than six-monthly) are recommended during the period of highest transmission.

During the past two years other operational programme changes have included using smaller localities rather than municipalities as the basic epidemiological unit; malacological studies to identify peak periods of transmission for more effective snail control; and attempts to improve sanitation and increase water supplies.

In most cases, following the implementation of water-resource development projects in Brazil, there has been no initiation of transmission. This is due in part to active case detection and treatment, but also to malacological surveillance and the use of snail control measures.

4.2 Countries where *S. haematobium* is endemic

4.2.1 Congo

The national schistosomiasis control project was initiated in October 1979 and covers the major *S. haematobium* endemic areas in the Bouenza, Niari, and Kouilou regions, where there is an estimated total population of 580,000. Among this population at risk it is estimated that 65% are infected.

The broad objective of the project is to reduce prevalence in all regions to below 8% using chemotherapy combined with snail control activities.

At the beginning of the programme surveys were made among schoolchildren, using the Nytrel filter technique (13-mm diameter) for the examination of 10-ml samples of urine. Up to 50 eggs were counted and the number recorded. Egg counts greater than 50 were recorded as > 50.

In areas where the prevalence among schoolchildren was greater than 10%, health education was given to all administrative and health authorities as well as to the villagers. Subsequently all residents were registered, houses numbered, and maps made. Urine specimens were examined and all persons found to be infected were treated with praziquantel. In areas where prevalence was less than 10%, control activities were postponed.

In the areas treated so far, prevalence has been reduced from 49.2%, in 1980, to 15.8%, in 1983. During the maintenance phase of control, special attention will be given to 5–14-year-old children
and, in order to keep reinfection rates as low as possible, examinations and treatments will be given at 6-monthly intervals.

A special study was made at N'kayi, the headquarters of the Bouenza region, where the population is estimated to be 38,000. In a school survey, nearly 90% of more than 1000 children were found to be infected, with a geometric mean of 186 eggs per 10 ml of urine. In May–June 1981, with the aid and support of local authorities, mass treatment with metrifonate was given: 97%, 90%, and 81% of the population received 1, 2, and 3 doses of the drug, respectively. Six months after treatment, 24,000 individuals were re-examined and 31% of them were found to be still positive. Subsequently praziquantel was used for treatment in the control project and 2½ years after the programme began the prevalence was estimated to be about 10%.

4.2.2 Morocco

A variety of epidemiological foci exist in Morocco, varying from old established, stable foci to the new foci created during the implementation of medium- and large-scale irrigation schemes that are expected to cover 1 million hectares (10,000 km²) by the year 2000. Because of these new irrigation schemes the number of notified cases of S. haematobium infection increased between 1966 and 1976. These schemes employ full-time and part-time immigrant workers who come mainly from areas where schistosomiasis is endemic.

The population at risk is estimated to be 650,000 people living in 16 of the 47 provinces; they are served by 85 health centres.

Planning for the national schistosomiasis control project began in 1976 and control was initiated in 1982. The objectives of the project include preventing new foci of transmission arising in irrigated areas that are as yet uninfected, containing new foci, and reducing prevalence by at least 50% in endemic areas.

The national schistosomiasis control project is integrated with other primary health care activities and supported by health centre staff assisted by microscopists trained to diagnose malaria and schistosomiasis. Funding is included in the 1981–85 development plans of the Ministry of Public Health as well as in the national plan for economic development.

Control operations include the treatment with metrifonate of all persons found to be excreting S. haematobium eggs (with re-examinations at 4 and 12 months after treatment), the reduction of
snail intermediate host populations at transmission sites using niclosamide, and health education.

Three methods of screening are employed:

(a) Selective screening: routine examination of urine samples of all those attending health centres;

(b) Intensive screening: by home visits undertaken by primary health care workers;

(c) Mass screening: during mass campaigns undertaken by mobile teams.

These screening techniques covered 13.2% of the population at risk in 1982 and 21% in 1983. In a 2-year period selective screening was used to examine 41%, mass screening 27%, and intensive screening 32% of the total number of persons examined. The prevalence as assessed by selective screening has fallen from 25.4% in 1980 to 7.3% in 1983.

The results of this primary health care approach to schistosomiasis control are encouraging.

4.2.3 Tunisia

The isolated foci of transmission in Tunisia associated with very limited water bodies in oases were ideal for attempting the eradication of *S. haematobium*. Parasitological and malacological surveys were made during 1970–71 which identified the central region between the Atlas and Gafsa mountains as the only endemic focus, with a population at risk of 150,000. Distribution of the infection was irregular, with up to 70% of the population being infected in some areas. Populations of *Bulinus truncatus*, the only snail intermediate host, were found to be highest during the warm months and very low in winter so that transmission was seasonal.

Control operations were directed at both the elimination of *B. truncatus* using niclosamide and the treatment of all infected persons with niridazole. Infected individuals were detected by sedimenting samples of urine.

Health education formed an integral part of the programme. Sanitation was not within the scope of the programme. Snails were easily eliminated by mollusciciding; *B. truncatus* was eliminated after a single treatment with niclosamide from almost 75% of sites while other sites required two or more treatments.

74
Repopulation of the vector snails occurred with decreasing frequency—in 40 of 440 sites in 1973 to only 1 (of 528 sites) in 1978. However, in 1981 and 1982 the number of observation stations was reduced along the irrigation canals and the *B. truncatus* population increased and the number of cases of *S. haematobium* infection rose from 23 in 1980 to 144 in 1982.

A large section of the population was treated; between 1972 and 1979 only 4% of diagnosed cases were not treated, the majority of these cases being elderly persons with low levels of egg output. The reservoir of infection after treatment was low but was supplemented by infection among expatriate Tunisian workers returning home for a holiday.

In 10 localities selected for periodic evaluation between 1971 and 1979, the overall prevalence of infection fell from 34% in 1972 to 2.5% in 1975 and 0.5% in 1979.

The experiences of this project show that even when there are very high levels of snail control and coverage with chemotherapy if untreated cases remain, or infected immigrants come to the area and snail intermediate hosts are still present in the water-bodies frequented by the local population, then a resurgence of transmission is likely to occur. However, the intensity of infection among new cases remains low and the morbidity associated with *S. haematobium* infection is infrequent.

### 4.2.4 United Republic of Tanzania: Zanzibar

Of the 600,000 persons who live on the islands of Pemba and Nguja, 45% are estimated to be infected with *S. haematobium*.

A pilot study to control *S. haematobium* infection in the village of Kinyasini on Ngua Island (population approximately 4000) was started in July 1981. The objective of the project was to reduce by 75% the prevalence of heavy infections (egg output greater than 50 eggs per 10 ml of urine), and by 50% the overall prevalence, in 2 years.

Water contact occurs during washing and bathing in streams and swamps but drinking-water is obtained almost entirely from taps and wells. Rice is cultivated extensively around the swamps and streams. Although transmission of infection probably occurs throughout the year, the peak is in the dry season between June and September.
The programme was undertaken by a health officer, 2 assistant health officers, 3 microscopists, 2 laboratory assistants, and a driver, all from the Ministry of Health. An extensive campaign was carried out to obtain the full support of the community.

Urine samples (10 ml) were examined using the Nytrete filtration technique; up to 50 eggs per 10 ml of urine were counted and recorded. Higher egg counts were recorded as > 50.

A standard dose of metrifonate was administered in selective population chemotherapy regimes during April and August each year when the schools were in session and transmission decreasing. The participation rate fell from 65.3% at the first treatment to between 50 and 57% in subsequent campaigns. Schoolchildren were treated four times and adults three times in two years.

Two years after the first treatment (and 3 months after the last treatment) it was found that among residents in the village aged 5–14 years, prevalence had fallen from 70.4% to 31.2%, and the prevalence of heavy infections (> 50 eggs per 10 ml of urine) from 35% to 11%; among adults, prevalence fell from 41.1% to 11.1% and heavy infections (> 50 eggs per 10 ml of urine) from 10.9% to 0.7%.

4.3 Countries where both S. haematobium and S. mansoni are endemic

4.3.1 Egypt

Past and present control activities reflect the magnitude of the ever-increasing problem of schistosomiasis in Egypt. The reasons for this include:

(a) A change from basin to perennial irrigation in Upper Egypt led to increased prevalence of S. haematobium.

(b) The building of the High Dam resulted in changes in water quality and water velocity in the Nile. This led to more stable snail habitats and Biomphalaria spp., previously restricted to the Delta, are now being found in Upper Egypt. The changed pattern of water flow may also have been responsible for the changing pattern of schistosome infections in the Delta—S. haematobium prevalence is decreasing, S. mansoni is increasing. The same phenomenon is observed for the intermediate snail host.

(c) The movement of refugees from the Suez Canal zone to the Delta in wartime resulted in their becoming heavily infected by
S. mansoni. Since they returned home transmission has become established because of the presence of Biomphalaria snails.

(d) The development of water resources and land reclamation projects have exacerbated the problem.

It is estimated that the population at risk of infection in Egypt is about 33 million persons. Major projects with an integrated approach using selective population chemotherapy and area-wide mollusciciding have been implemented in Upper Egypt.

1. Fayoum. This project is now in the maintenance phase. The prevalence of S. haematobium infection was reduced from 45.7% in 1968 to 6% in 1975. Surveillance of the population of 1.2 million indicated a subsequent rise in prevalence that is now under control.

2. Middle Egypt. The population in this area (4.5 million) is screened annually and metrifonate is given to those infected; 3 doses of 10 mg/kg are administered at 2-week intervals. Prevalence dropped from 29.4% in 1977 to 11.5% in 1983.

3. Upper Egypt. The population (5.1 million) is screened annually and metrifonate given at the same dosage as that used in Middle Egypt. Prevalence dropped from 26.4% in 1980 to 16% in 1983.

4. Giza project. The population (2.4 million) is screened annually. Treatment is with metrifonate (dosage as in Middle Egypt) and with praziquantel—40 mg/kg given as a single dose for cases of S. mansoni and mixed infections. This project began in 1983.

5. High Dam Lake. Measures to prevent transmission started in 1974 when Bulinus truncatus was found to be widespread in the lake. The population consists of about 7000 fishermen who are examined regularly. Positive cases, usually with S. haematobium infection, are treated with praziquantel before being permitted to work on the lake.

6. West Nubaria project. Preventive measures to be carried out on 810 km² of newly reclaimed land will include pre-settlement screening and treatment of positive cases with praziquantel. This project will begin in 1985.

7. Suez Canal area. Mainly mixed infections occur in this area. Control is planned to begin in the governorates of Damietta, Port Said, Ismailia, and Suez in 1985.

8. Nile Delta. Within an area limited to about 22 villages (one district with 170,000 inhabitants) a project was carried out in 1983.
that aimed to screen the schoolchildren annually and to treat positive cases with praziquantel, given in a single dose of 40 mg/kg.

4.3.2 Mali

Mali was one of the first African countries to adopt primary health care as the basis for its national health policy; schistosomiasis control is included in the country’s primary health care programme. A small specialized schistosomiasis control team cooperates with the primary health care services for tasks needing special equipment and knowledge. An attempt has been made to develop a programme to provide specialized schistosomiasis control that coordinates with the primary health care system.

Although schistosomiasis is widespread, control is directed towards only four population groups: (a) those near small dams on the Dogon plateau; (b) those around Niono and Kolonotom (Niger irrigation project); (c) the Selingue dam population; (d) the population in the Baguineda irrigation zone.

The aim of control is to reduce the prevalence of *S. haematobium* infection to below 20%. Control operations consist of examining about 100 persons per village; if prevalence is greater than 20%, specialist teams initiate health education, identify intermediate hosts and transmission sites, and carry out focal molluscciding for 6 months prior to chemotherapy of the population with praziquantel. If 75% or more of the population are positive at the first examination then mass chemotherapy is administered; if 20–75% are positive, then only those who are infected are treated (selective population chemotherapy).

Preliminary results indicate that, despite vector control and an improvement in environmental hygiene, repeated treatment campaigns are needed to reduce the prevalence to less than 20%. The influence of immigration of infected persons into these areas has yet to be assessed.

4.3.3 Sudan

Schistosomiasis due to *S. mansoni* exists mostly in major irrigation schemes and the southern regions of the country with some foci of *S. haematobium*; *S. haematobium* exists mostly in Western Sudan in rain pools and in small pump schemes in Northern Sudan and the Blue Nile province.
The national control programme for schistosomiasis was formulated in 1979 as part of the Blue Nile health project, the aims of which are the prevention and control of water-associated diseases using an integrated comprehensive strategy. The project is made up of two large schemes (Gezira and Rahad).

(1) Gezira scheme. Baseline data on prevalence rates, snail populations, behavioural practices, irrigation practices, weeds, etc., have been collected from the study zone (50,000 persons). Praziquantel was used for mass treatment in villages with prevalence rates of more than 40%; in villages where the prevalence rate was lower, only infected persons were treated (selective population chemotherapy). Further measures taken included focal molluscciding with niclosamide, weed removal in some areas, and the introduction of health education programmes. The overall prevalence rate dropped from about 50% to 11% in one year. It is expected that the entire population of the 8100-km² scheme will be covered in 5 years in a phased programme.

(2) Rahad scheme. In the relatively new Rahad scheme the emphasis is on the prevention of transmission. The population at risk (100,000 persons) is subjected to periodic surveillance; all infected subjects are treated with oxamniquine or praziquantel, and focal molluscciding with niclosamide is carried out in snail breeding places. Efforts have also been made to improve sanitation facilities and water supply systems.

4.4 Countries where S. japonicum is endemic

4.4.1 China

The control of schistosomiasis as a national programme started in 1955. A directing board was created by the Central Committee of the Chinese Communist Party to coordinate the activities of different departments, to set up control policies, and to provide guiding directives. Local committees at all levels and provincial institutes of schistosomiasis were established and strengthened.

Comprehensive measures have been advocated, including chemotherapy and snail control which is closely integrated with agricultural production. Mollusicides have been used occasionally.

Considerable progress in control has been made over the years, and of 348 counties where the infection was known to be endemic, 56 are in the surveillance phase, 191 in the consolidation phase, while
101 are still in the attack phase. Many antischistosomiasis hospitals have been closed or reorganized as morbidity due to *S. japonicum* infection has decreased.

The number of infected persons is currently estimated to be 1 million (one-tenth of the original number) and the snail-infested area has been reduced to one-fifth of its original size.

The greatest remaining problems are in high mountainous regions where the population is sparse and snails breed in seepage water, and in lake regions where new breeding places for *Oncomelania* spp. are constantly being created.

4.4.2 **Philippines**

*S. japonicum* infection continues to be a serious public health and socioeconomic problem in central and southern Philippines. An estimated 700,000 people are infected out of a total of about 4 million persons exposed to the risk of infection in 141 municipalities (barangays) in 22 provinces.

Until very recently, the Schistosomiasis Control and Research Service of the Ministry of Health has been in charge of the vertical control programme based on the classical four-pronged approach: (a) control of the snail intermediate host through environmental modification followed by terminal molluscidation; (b) case-detection and treatment of cases; (c) environmental sanitation; and (d) health education. Because of the magnitude of resource requirements and the need for coordination and integration of efforts of various government agencies in the control of the disease, the National Schistosomiasis Control Council was created in 1976. Through this Council, the Government has made schistosomiasis control an integral part of all foreign-assisted rural development programmes in endemic areas. Close collaboration between the National Irrigation Administration and the Schistosomiasis Control and Research Service has been a prominent feature of the control programme.

Recently, the development of more effective, less toxic, and orally administered drugs against schistosomiasis has greatly facilitated and redirected the control efforts. With the use of praziquantel in two separate field trials, a very significant reduction in the prevalence rates of infection was obtained (from 43% to 17% in one trial, and from 22% to 12% in the other). Serial clinical examinations on 116 persons one year after treatment demonstrated that the liver, spleen,
and combined liver and spleen enlargement rates dropped from 96% to 70%, 13% to 8%, and 13% to 8%, respectively.

A control programme based on chemotherapy was launched in the province of Leyte in 1981. To date, about one-quarter of a million individuals have been examined and more than 50,000 of them treated with praziquantel.

Following a directive from the Ministry of Health, the national chemotherapy programme for schistosomiasis control was fully integrated into the health services at the regional and provincial levels in 1984. The control programme is now under the direction of the regional health director in each endemic area. A programme management committee with the provincial health officer as chairman directly supervises and controls the programme together with the staff of the schistosomiasis field teams.

5. A STRATEGY FOR MORBIDITY CONTROL

Until recently the strategy for schistosomiasis control was aimed at reducing transmission by diminishing the snail population; as this method became effective, morbidity in the human population was slowly reduced, and, in the long term, the complete eradication of the parasite might have been achieved. However, in only a few small foci with unusual epidemiological characteristics was transmission completely halted while, in other areas, general economic development, associated with the provision of improved water supplies and sanitation and snail control, has led to prevalence being reduced to low levels.

A major change in strategy became possible with:

(a) a better understanding of the epidemiology of schistosomal disease, and recognition that the frequency of urinary tract abnormalities and hepatospleno-megaly was directly related to the intensity of infection and prevalence, both being high in the 10–14 years age group;

(b) the development of simple quantitative diagnostic techniques suitable for field studies; and

(c) the development of new drugs suitable for use on a large scale.

At present, the primary objective of schistosomiasis control is to reduce or eliminate morbidity, or at least serious disease. Since morbidity is caused by the eggs deposited in tissues, a reduction or
elimination of the adult worms will reduce the risk of morbidity developing. The number of worms present can be estimated by counting the number of *S. mansoni* or *S. japonicum* eggs per gram of faeces or the number of *S. haematobium* eggs per 10 ml of urine. Quantitative parasitological diagnostic techniques now in common use make it possible to detect with reasonable accuracy any reductions in prevalence and/or intensity of infection.

While several methods are now available for the control of schistosomiasis, there are certain basic requirements that must be fulfilled before a control programme can be implemented and continued through to the maintenance phase (see section 5.5):

(a) Recognition of the importance of the disease and commitment at the national and local levels to effect control. Such commitment is important among both those responsible for the allocation of resources and the individuals who would be involved in a control programme.

(b) Adequate organizational and managerial structures. These will vary according to the health services of the different countries but there must be a national capacity to collect basic data and to plan, implement, and evaluate schistosomiasis control. International cooperation may be necessary where national capabilities for assessment of the epidemiological situation, planning, and implementation of control are inadequate.

(c) Availability of manpower resources. A capacity for health education and training at the primary health care level should be developed. A small nucleus of specialists is required at the central level. These should be supported by technicians with training in the various methods and techniques used in epidemiological studies of parasitic diseases.

(d) Availability of financial resources. If external funding is obtained initially, this is unlikely to continue indefinitely and governments should pursue a policy of self-reliance as soon as possible.

5.1 Operational approaches

Morbidity control focuses on people as the definitive host and the primary reservoir of infection. For this reason activities such as health education and chemotherapy should be emphasized. This approach does not mean that snail control measures should not be
used in any phase of control, if appropriate, or that improvements in sanitation, water supplies, and environmental management should not be considered.

5.1.1 Operational phases

In the previous Expert Committee report (19), three main phases of schistosomiasis control operations were outlined.

(1) Phase 1 (planning) is the period when the collection of necessary epidemiological data takes place, a national plan of action is prepared in which the quantitative goals of the control programme are defined according to the priority given to the problem, a feasible operational approach is decided upon, and appropriate resources are allocated to the programme.

(2) Phase 2 (attack/intervention) is the period of active intervention. The operations are intensive and continually evaluated. In this phase a rapid reduction in prevalence and intensity of infection can be anticipated. This phase is usually shorter than the first phase. Preparations for phase 3 should be started at the beginning of phase 2.

(3) Phase 3 (maintenance) is a protracted follow-up period during which maintenance measures will be necessary in most situations; fewer resources will be required and they will be used to support established facilities and primary health care for surveillance and monitoring.

Programmes for morbidity control must be supported by efficient laboratory services, including reliable microscopic diagnosis, and data collection and analysis capabilities, and must be able to muster resources for health education.

5.1.2 Types of operational approach

The primary operational goal of the active intervention phase of schistosomiasis control using chemotherapy is the rapid coverage of the entire target population. The success of a control programme is not so much dependent upon the methods employed, but rather on its managerial and supervisory aspects.

There is a wide choice of operational approaches according to national needs and capabilities. It is desirable that intensive control activities should be undertaken by mobile teams working in
association with primary health care workers. Schistosomiasis control of populations at risk as part of agricultural and water resource development schemes is now more feasible than in the past (see section 1.4.3).

Programmes to reduce morbidity should orient their operations to achieve complete coverage of the section of the population of school age. Surveys to diagnose and treat children in schools can be undertaken rapidly and efficiently. The degree of coverage of the school-age population will depend on the level of school attendance in any given area.

Operations for the control of morbidity due to schistosomiasis can be integrated with other operational programmes of high priority. In *S. mansoni* endemic areas, schistosomiasis control should be closely linked, if not integrated, with the control of intestinal parasitic infections. Control of *Schistosoma haematobium* (more feasibly than *S. mansoni*) may be linked with immunization programmes, nutritional and maternal and child health activities, tuberculosis, leprosy, and sleeping sickness surveys, as well as the control of diarrhoeal diseases. Schistosomiasis control may often be integrated with other programmes that require systematic repeated surveillance activities.

### 5.2 Operational components

#### 5.2.1 Health education

Health education is a continuous process in endemic countries; it should be started before the introduction of control operations and should continue beyond the intensive phase of operations. In programmes oriented to achieve morbidity control, health education is essential from the outset. One responsibility of the field staff of the control programme is to communicate health information as well as health education.

Community participation is essential for chemotherapy to be successful and no campaign should be undertaken without extensive preparation so that all those involved understand their role in the transmission of the disease and the benefits that can be obtained from fully cooperating with the programme. Health education approaches are outlined in section 3.1.
5.2.2 Delivery systems for chemotherapy

The selection of a delivery system for antischistosomal chemotherapy should be based on a sound understanding of the epidemiology of schistosomiasis as well as the effectiveness of the drug to be used. The basic elements of any chemotherapy delivery system are personnel, diagnostic techniques and associated materials, drugs, logistic support, and data management.

5.2.2.1 Mass treatment. Strictly speaking, this term refers to the treatment of entire populations without prior individual diagnosis. The decision to employ mass treatment must be based on adequate epidemiological data indicating that a very high proportion of the population is infected. The sampling frame and design of this approach are critical and should be based on the smallest administrative units.

Case-detection costs are low and restricted to preliminary sampling to establish a high prevalence; drug and delivery costs are high but large effects on morbidity and transmission can be expected (see Table 5).

Table 5. Comparison of national costs and benefits of different chemotherapy delivery systems

<table>
<thead>
<tr>
<th>Delivery system</th>
<th>Costs</th>
<th>Effects on</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case detection</td>
<td>Drug</td>
</tr>
<tr>
<td>Mass treatment</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Selective population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>chemotherapy</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Selected group treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>— total</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>— infected</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Targeted</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

5.2.2.2 Selective approaches. A number of possible approaches to the treatment of selected groups within endemic populations are available (see Annex 2).

(1) Selective population chemotherapy. In this approach, urine and/or stool specimens from the entire population of an area are examined. Only persons excreting Schistosoma eggs are treated.
Case-detection costs are high but drug costs are lower than with mass treatment. Delivery costs may also be lower than with mass treatment. A high level of morbidity control can be achieved and the effect on transmission will be only a little less than with mass treatment if the diagnostic test used to identify infected persons is sensitive.

(2) Selected group treatment. This approach is a variant of selective population chemotherapy. As peak prevalence, intensity, and morbidity are generally found in the younger age groups, treatment can be given to these groups—either to the entire group or to all those infected.

If a high proportion of children go to school, this approach is probably the easiest to organize. When the whole group is treated, case-detection costs are limited to those of the survey defining the epidemiological status of the area; drug delivery costs will be lower than in the regimes described above. Although the overall effects on morbidity and transmission will be less than with mass therapy, the effects will be great in the age groups at greatest risk among the individuals who are responsible for much of the environmental contamination.

On the other hand, if only infected persons in the group are treated, case-detection costs are higher but drug costs are lower than when all the groups are treated.

These two approaches probably have the greatest benefit relative to cost.

(3) Targeted chemotherapy. This is the term it has been suggested that should be used to refer to a method for treating individuals with high levels of egg output who are at the greatest risk of developing disease. Reports from a small field trial of this approach suggest a reduction in morbidity; however, it remains a theoretical approach that has been inadequately tested on a large scale.

(4) Phased treatment. The selective population chemotherapy approach has been employed more frequently than the others, but in countries where the prevalence varies from locality to locality a more flexible approach may be required. While the approaches outlined above should all be considered independently, various combinations, in sequence (phased treatment), might also be envisaged. Thus in areas of very high prevalence mass treatment might be followed, when prevalence and intensity of infection have been reduced, by selective population chemotherapy and
subsequently by selective group treatment. This method appears to provide for the most economical use of drugs.

5.2.2.3 Re-treatment schedules. With the strategy of morbidity control it is anticipated that transmission will continue after large-scale treatment, but for some time it will probably be at a lower level than before. Further treatments will be required to maintain the control of morbidity. While chemotherapy is playing an increasing role in controlling schistosomiasis, it is apparent that transmission will continue; however, complementary activities can delay the need for re-treatment. In addition, it is known that the rate of reinfection is higher in children and that clinical disease is unlikely to develop in less than three years. The rate at which prevalence and intensity of infection increase will depend on:

(1) The number of persons remaining infected after treatment, which is in turn dependent on:
— the pre-treatment level of endemicity;
— the operational approach used;
— the degree of population cooperation in providing material for case detection and in accepting complete courses of therapy;
— the "cure" rate;
— the number of deferred treatments due to pregnancy, ill health, etc.;
— the extent of population movement and immigration of infected persons.

(2) The rate of reinfection, which is itself dependent on:
— the extent of water contact, which may be inversely proportional to the availability of a safe, adequate, and reliable water supply;
— the extent of faecal and/or urine contamination in the environment;
— the size of snail intermediate host populations and the seasonality of transmission;
— the rate of infection among animal reservoirs, especially in the maintenance of transmission in areas where S. japonicum is endemic.

The availability of diagnosis and treatment at the first level of the health delivery system provides important support to intensive
control efforts and will be essential during the maintenance phase of schistosomiasis control.

During programmes to achieve morbidity control re-treatment would be undertaken when the intensities of infection in the community reach levels that, if untreated, would be likely to cause disease. More information is required on this aspect of control from different endemic areas and it could be obtained by the careful monitoring of the relation between morbidity and infection intensity and duration following chemotherapy programmes. Such applied field investigations should be carried out by control programme groups that are associated with research groups appointed to investigate any specific problems that are encountered.

5.2.3 Water supply

Interventions related to the supply of safe water are intersectoral. The agencies responsible for water supply should be informed of their role in promoting disease control. The endemic areas where the prevalence and intensity of infection are initially high or where they remain high after direct intervention are ideal sites for the provision of adequate, reliable, and well-maintained water supplies. In addition, laundry and shower units maintained by the community should be installed. Health education and community participation is necessary if maximum benefits are to be obtained.

5.2.4 Snail control

Chemotherapy campaigns may be supported by a well-planned snail control programme. In endemic areas with a high prevalence rate and year-long transmission, the results from chemotherapy programmes may be enhanced if transmission is reduced by a period of snail control before treatment is started.

(1) Delivery systems. Apart from the conventional means of applying molluscicides using hand-operated or pressure sprayers, automatic and semi-automatic dispensers, etc., two other, more novel, methods of delivery have been tried in the past few years. The first of these, the aerial application of molluscicides, can now be regarded as generally ineffective.

The second, the concept of controlled, slow-release application, has been explored during the past decade. The attractions of this approach include a substantial reduction in cost, greater operational
simplicity, less harm to the environment, and the destruction of free-swimming larval stages of the parasite; it is particularly valuable in focal transmission control in static water-bodies. In spite of these attractive features, no slow-release formulations of molluscicides are commercially available.

(2) Mollusciciding. In some endemic areas population-based chemotherapy programmes may be supported by mollusciciding operations together with other methods of control. If the mollusciciding operations are effective, there can be a rapid interruption of transmission.

Blanket mollusciciding may be most cost-effective in sophisticated irrigation schemes with excellent water management and widespread and intense transmission and also in naturally occurring, flowing, water-bodies. On the other hand, focal mollusciciding operations should usually be restricted to places that are used extensively by the population for domestic purposes and to nearby habitats. Such sites are known to the local people and their position can be confirmed by the evidence of frequent access. Simple maps showing the location of transmission sites should be prepared and kept up to date. Such maps should also be correlated with prevalence rates in the local population since mollusciciding should not normally be undertaken at sites used by populations with a low prevalence of infection.

As a general rule, in still water-bodies the molluscicide should be applied within a radius of at least 15 metres around the transmission site. In flowing-water habitats the mollusciciding procedures are a little more complicated. Simple solution dispensers that can be made locally may be required and should be sited just upstream of the main water-contact places. The frequency and timing of molluscicide applications will depend upon the type of water-body and the pattern of transmission.

A detailed description of how to apply molluscicides is given in a WHO monograph (15). Manufacturers will also provide instructions on request.

5.3 A primary health care strategy to control morbidity due to schistosomiasis

As the epidemiology of schistosomiasis varies from one endemic country to another, so the managerial and operational structure of
schistosomiasis control activities will vary. The simplicity of the diagnostic techniques, the safety and ease of administration of oral antischistosomal drugs, the use of snail control measures based on specific epidemiological criteria and precise data collection and analysis, permit schistosomiasis control activities to be adapted to any level of the health care delivery system. Schistosomiasis control activities to reduce morbidity can be expected to be successful in primary health care programmes, particularly in areas where *S. haematobium* is endemic.

The rationale behind the primary health care approach is to stimulate the active involvement of the community and to facilitate the introduction of and support to the technical and medical interventions of specialized mobile teams or personnel. Through primary health care at the community level the progress of interventions directed against schistosomiasis can be monitored.

5.3.1 *Tasks of the primary health care worker*

The reduction in morbidity due to schistosomiasis through primary health care will involve data collection for assessment and evaluation, treatment and follow-up, health education, sanitation, and community participation.

A primary health care worker should collaborate with the specialized team during the preparation of a control programme in a community by assisting in the initial diagnostic and treatment surveys. In direct association with the specialized mobile team or trained personnel, he or she may undertake parasitological diagnosis and treatment with antischistosomal drugs.

After the initial survey and treatment have been completed, the primary health care worker will continue to monitor the local situation and send periodic reports via the supervisory channels. For this purpose it is critical that, at the field level, an appropriate data collection format is carefully worked out so that data can be recorded clearly and transmitted via the administrative hierarchy to those responsible for allocating resources. The data must also be analysed and interpreted by primary health care supervisors who will decide upon any operational changes that may be necessary.
5.3.2 Health education

The primary health care worker is the most important provider of health education in the community, educating its members on their role in the transmission of schistosomiasis, on the impact it has on their daily lives and life-style, and on their responsibilities in the elimination of the causes of schistosomiasis. Simple, practical and durable materials that can be used by primary health care workers for this purpose should be developed.

Sanitation, water supply, and health education are all important aspects of schistosomiasis control, but their implementation is usually the responsibility of governmental agencies other than the ministry of health. The primary health care worker may contribute constructively by encouraging community participation in the installation of sanitation and water supplies. While his or her knowledge of the customs and habits of the community may be useful in deciding upon the sites for washing facilities and wells, and upon the modification of water-bodies for recreation, etc., the primary health care worker should be specifically trained for the clearly stated objectives of health education in the community.

5.3.3 Diagnosis of schistosomiasis at the primary health care level

The parasitological techniques available at present can be used by all levels of health worker and even by community members who have received a minimal amount of training. The costs related to parasitological diagnosis may consist of simply the initial capital investments, with low long-term renewal costs. Simplified microscopes have been developed and are now being evaluated. The cellophane faecal thick-smear is the technique of choice to diagnose *S. mansoni* and *S. japonicum* infections. If no microscope is available, the slides can be prepared and transported to a central laboratory or kept for examination by a mobile technical team.

The syringe filtration technique using nylon mesh (Nytrel) filters is appropriate for urine examination since all the material is reusable. Alternatively, semiquantitative indirect techniques such as reagent strips to detect haematuria will help in identifying heavily infected individuals and also in assessing the impact of the control efforts on morbidity due to *S. haematobium* infection. The primary health care worker may also record the prevalence of gross haematuria in schoolchildren or in the community, for the purposes of epidemiological surveillance.
5.3.4 *Chemotherapy*

Effective treatment of schistosomiasis should be organized at the community level to control morbidity, and to have maximal impact on transmission it should be given to all infected persons with the minimum delay and should be administered by medical or specialized trained personnel.

Theoretically, the availability of treatment through primary health care workers might contribute to the risk of the appearance of drug resistance. So far, resistance to praziquantel has not been observed, and, at present, resistance to oxamnique does not affect large-scale treatment programmes. Antischistosomal drugs may, however, deteriorate rapidly if they are not stored properly, and this may lead to difficulties if adequate storage facilities are not available at the community level. At present, the unsupervised use of drugs by primary health care workers is not recommended until this is justified by further experience with the available antischistosomal drugs. Treatment within primary health care should be restricted to the health facilities and personnel at the first referral level.

5.3.5 *Snail control*

A primary health care worker or sanitarian may be trained to recognize specific locations in and around the community where schistosomiasis is most likely to be transmitted. Such identification may be based on the use of a water-contact point by persons for washing clothes, bathing, recreation, or urination or defaecation, especially by persons who have clinical manifestations of schistosomiasis (i.e., haematuria), or on the observation that intermediate snail hosts are obviously present. The application of molluscicides at the village level, by primary health care personnel who have received a minimal level of training, is being evaluated. Environmental modification of water-contact sites and snail habitats should be carried out with community participation.

5.3.6 *Support systems for primary health care*

It cannot be overemphasized that the process of information transfer from the primary health care worker at the community level to the appropriate supervisors in the ministry of health for evaluation and response should be clearly laid down.

92
A national schistosomiasis control programme should support, coordinate, and supervise all schistosomiasis control activities at the primary health care level. The organization of training courses for primary health care workers should be part of the national schistosomiasis control programme. The preparation of a training manual and education materials will be necessary. It is also advisable to organize periodic training and evaluation seminars.

5.3.7 Linkages between primary health care and development programmes

Schistosomiasis is spreading within agricultural and water-resource development projects. At the community level the primary health care worker may be the first person working in the health field to become aware of the implementation of such projects. A mechanism for reporting such new projects to supervisory personnel should be provided.

5.4 Factors influencing the choice of operational approaches

5.4.1 Available control approaches

Operationally, in a control programme, there are two main aims—the control of transmission and/or the control of disease. The latter objective should now take precedence. However, while morbidity control of schistosomiasis is usually technically and operationally feasible there are financial, organizational, and managerial constraints that will determine which operational approaches are selected. Morbidity control may rely on such operations as chemotherapy, health education, snail host control, water supply, and sanitation.

In endemic countries with an adequate health care delivery infrastructure, schistosomiasis control may be implemented through health centres and primary health care facilities. In particular, those operational approaches that will include all the population of school age are the most promising for morbidity control programmes.

The choice of operational approach will be determined by the rational use of available resources, and some flexibility is desirable. If mobile teams cannot be used, then health centre staff may be trained to carry out systematic periodic selective population chemotherapy or mass treatment (if the prevalence and intensity of infection are high) in nearby schools.
There are two main aims of transmission control. The first is to prevent the contamination of potential transmission sites with schistosome eggs by reducing the egg output of infected individuals with chemotherapy and/or by the use of latrines. The second is to prevent the frequent exposure of the population to cercariae-infested water by destroying snail populations and reducing contact with water by, for example, the provision of an alternative safe water supply.

The characteristics of operational components may be evaluated in terms of the local endemic area, and should include specific epidemiological, ecological, socioeconomic, and cultural factors. It will be necessary to envisage at an early stage a multiplicity of constraints.

5.4.2 The limitations of operational phases

5.4.2.1 Intervention phase. The aim of this phase is to reduce rapidly all the indices of infection by preventing the development of disease and by reversing early disease processes. Chemotherapy is the essential method used. Transmission will be reduced, but the level of infection remaining after chemotherapy, together with other epidemiological indications, will determine the rate at which prevalence and intensity of infection will again increase. This rate of increase can be reduced by limiting the exposure of the population to infected water (i.e., transmission control) during the maintenance phase.

5.4.2.2 Maintenance phase. Where transmission sites are well defined, small, and close to villages, focal and seasonal snail control may be an appropriate method of preventing infection.

In areas where massive immigration of infected persons occurs regularly and where examination and treatment of these persons is logistically difficult, a carefully planned snail control operation may be required.

Where there are no safe water supplies and where snail control cannot be implemented, re-treatment programmes will be needed. However, since participation for repeated treatment may decline markedly, every endeavour should be made to incorporate alternative intervention components.

Regarding water supplies, a communal standpipe does not necessarily eliminate contact with infected surface water, but the
provision and use of simple laundry units and showers (see section 3.6.2) can substantially reduce exposure. During this International Drinking Water Supply and Sanitation Decade, the provision of communal laundry and shower facilities, as part of the water distribution system, should be encouraged.

5.4.3 Agricultural development areas

The risk of schistosomiasis is sometimes neglected during the formulation of development projects. Many agricultural and water-resource development schemes are supported or financed by bilateral aid agencies and multilateral sources such as UNDP, FAO, and the World Bank. Alerting these agencies to the possible risks of schistosomiasis is not enough to guarantee that there will be adequate planning and investment for control. They must be convinced that morbidity control is feasible and that the political will to put it into practice exists within the country concerned, as well as the necessary basic technical and organizational capacity.

5.4.4 Urban areas

Urban transmission of schistosomiasis is an ever increasing problem of development owing to the migration of infected persons from rural areas. Diagnostic services and treatment should be provided at the first level of the urban health care delivery system and these should be supported by efforts to identify the sites of transmission and to eliminate them by environmental modification and mollusciciding if necessary.

5.4.5 Personnel and political commitment

The availability of personnel for either of the above intervention procedures will depend largely on the political commitment to the control of schistosomiasis. Careful attention must be given to the training of both primary health care and programme personnel so that they can accomplish the multidisciplinary tasks that may be involved.

5.4.6 Costing base

The costing base for schistosomiasis control programmes is still incomplete, but as experience in national control programmes
increases the necessary data will become available. Comparison between countries may not be realistic because of differences in exchange rates, cost-of-living indices, employment regulations, and salary structure. In endemic developing countries it is realistic to distinguish between hard currency costs (foreign exchange) and local costs. The cost of all the human resources for a national control programme should ultimately, if not initially, be borne locally.

In most control programmes, in which the costs of operation have been carefully analysed, the drug costs make up 10–30% of the total cost. The purchase of the drug usually represents an expenditure in a hard currency and such currencies may not be readily available. The World Health Organization and the manufacturer of praziquantel have made a unique agreement that WHO may purchase the drug at a special low price when it is to be used in large-scale national control programmes; this agreement has been extended to include purchases by other agencies for similar purposes. However, the cost of the drug should not be the factor that determines its proper use. If funds are restricted it may be appropriate to limit control operations to smaller geographical areas or affected communities instead of using the drug indiscriminately over a large area.

The cost of supplies and equipment for diagnosis, using the quantitative techniques that are now recommended, is in the range of US$0.01 or less per person. It is recommended that WHO should make every effort to obtain lower prices for national control programmes.

5.5 Maintenance and evaluation

With adequate chemotherapy both the prevalence and the intensity of infection can be rapidly reduced to levels that are unlikely to be associated with morbidity, but it is more difficult, and may not be necessary or economical, to reduce levels further. However, a maintenance programme is needed to sustain these levels and for this a number of requirements must be fulfilled:

(a) continued acceptance of schistosomiasis as a potential local or national problem;
(b) the establishment of a national socioeconomic and health development policy to include schistosomiasis;
(c) political and popular support for the policy;
(d) availability of the relevant and appropriate staff and the necessary equipment and supplies.

It cannot be overemphasized that it is important to have available an effective administration, as well as suitable organizational and managerial structures for the planning, implementation, and evaluation of the maintenance phase control activities.

5.5.1 Maintenance of control

The maintenance phase of programmes aimed at the control of morbidity should have specific objectives. Unless the minimum acceptable levels of prevalence and intensity of infection are defined, unnecessary interventions may continue. Repetitive large-scale chemotherapy is not a cost-effective way of achieving and maintaining transmission control in most endemic countries.

The maintenance phase will be implemented by the general health care delivery system. Personnel at the peripheral level, including primary health care workers, should be trained for specific tasks related to schistosomiasis. This phase includes continued health education, maintenance of water supply and sanitary services, community participation, and, where appropriate, snail control. All peripheral laboratories in first level health facilities and first level referral hospitals should have microscopes that can be used to diagnose schistosomiasis and to maintain passive case-detection.

The personnel who may have been involved primarily in schistosomiasis control should continue in this field, but should also be retrained for other disease control activities, e.g., control of intestinal helminths.

5.5.2 Evaluation of control

In public health orientated schemes, the effect of intervention must be monitored to ensure that the approaches used are appropriate, to detect any early resurgence of transmission that would require investigation, and to justify costs.

Monitoring by field teams ensures continuing evaluation, but an independent group—perhaps university-based—should be available to make periodic assessments and be responsible for investigating problems that arise during control. Both groups would be involved in parasitological and clinicopathological evaluations.
5.5.2.1 Evaluation of operations. A programme should have an operational target in each area of control; for example, targets in the areas of population awareness, the coverage of the population, and level of community participation. The success of the programme can be reliably evaluated by assessing whether or not these operational targets are achieved, and not solely by assessing the availability of the required supplies and equipment, transportation, or personnel.

(1) Operational efficiency. Immediate parasitological diagnosis and treatment reduce transportation costs and result in a high compliance rate. School-age children are the priority group for diagnosis and treatment, and school surveys may be carried out rapidly if they are carefully planned and well organized.

Previous planning of all surveys is essential since it will ensure full community cooperation and will expedite survey procedures.

(2) Efficiency at the work-bench. An efficient field operation will promote community cooperation. All aspects of a survey, such as the census, collection of specimens, examination of specimens, and subsequent treatment of infected persons, must be carried out efficiently and with the least possible delay.

It is suggested that diagrams are made of the planned layout of the work-benches, etc. Check-lists of equipment are useful so that no equipment or supplies are missing when the team arrives in the field.

5.5.2.2 Parasitological evaluation. Prevalence of infection is the most easily determined parasitological index, but it is not reliable in areas where there is a considerable degree of population movement and immigration of infected (or uninfected) persons. With new quantitative techniques, the intensity of infection can be readily determined, but the result is subject to the same error as for measurements of prevalence. To calculate both indices, data from newcomers to the area should be reported separately from data obtained from the more stable resident population. The intensity of infection can be reported in different ways; one simple and convenient way is the classification of egg output. The results from different age and sex groups should be given when possible (see Annex 1).

An assessment of the incidence of new infections will involve the re-examination after one year, of individuals who were originally negative, in order to ascertain how many have become positive; this
process requires a better system of data recording than does the assessment of prevalence and intensity of infection.

Parasitological data obtained from individuals who routinely attend hospital (in- or outpatients) and health centres can be used as a supplementary check. Data such as age, sex, and place of residence of those attending clinics are invariably recorded but are rarely analysed.

Quality control. Quality control of the work of the microscopists requires patience and tact. Quality control becomes increasingly important as prevalence decreases and as the proportion of negative results increases.

5.5.2.3 Evaluation of morbidity. Surveys to monitor changes in the rate of liver and spleen enlargement in children in areas endemic for *S. mansoni* infection must be carefully planned, but results from areas where splenomegaly is commonly caused by conditions other than schistosomiasis must be interpreted with caution.

Changes in the frequency of proteinuria and haematuria in areas endemic for *S. haematobium* infection can be determined by the use of reagent dip-sticks, while a reduction in haematuria or dysuria can be determined by observation or clinical history. The current use of ultrasound in two areas in East Africa may provide important information on the relationship between the levels of egg output and urinary tract deformities as well as the reduced frequency of the latter following control.

5.5.2.4 Evaluation of chemotherapy. The importance of using quantitative parasitological techniques has been emphasized in relation to the evaluation of the effect of treatment. If the prevalence and intensity of infection are not reduced after treatment then the following should be investigated:

- **(a)** The shelf-life of the drug. Drugs should not be used after their expiry date. Metrifonate has a shelf-life of 2 years if it is stored properly; the shelf-lives of oxamniquine and praziquantel are at least as long.
- **(b)** Operational failure. Effective supervision is necessary at all stages of a control programme.
- **(c)** Participation. The reasons for poor population participation should be identified and corrected while attempts should be made to promote cooperation.
(d) Resistance of the parasite to the drug. At present, this is not a problem in control programmes (see section 3.3.6).

5.5.3 Applied field research

The adaptation of operations to deal with unforeseen problems can be aided by the use of applied field research. The use of small-scale applied field research activities in national control programmes is important. These schemes are useful to encourage the necessary experimentation and innovation, test new methods and technologies, and verify the impact of intervention. They should be considered to be an essential programme element. If the national control programme does not have an independent research unit, the establishment of joint field research activities with national research institutions and implementing agencies is desirable.

5.6 Intersectoral cooperation

Effective control of schistosomiasis requires intersectoral coordination and collaboration. National intersectoral committees in Egypt, Ethiopia, Kenya, the Philippines, and Sudan are coordinating efforts to control schistosomiasis. The Expert Committee recognized the potential of these national bodies; they might be considered as models to be modified in other endemic countries according to national needs and priorities.

The agencies responsible for the specific development activities that influence the introduction or spread of schistosomiasis should be provided with recent data by the ministry of health on the distribution of schistosomiasis as well as the availability of resources for control.

Close coordination and collaboration between agricultural development agencies, particularly irrigation and schistosomiasis control programmes has proved to be a prerequisite for effective control in some countries, e.g., Egypt and the Philippines.

The changes necessary to incorporate health and environmental safeguards into water-resource development projects may require the introduction of a new organizational framework or the restructuring of existing organizations. Collaboration and coordination between institutions may contribute to the strengthening of the managerial capacity within organizations, improve planning and managerial processes, and strengthen the commitment
of each institution to introduce and maintain control of water-borne diseases. The advisory powers of national coordinating committees would include the possibility of making recommendations to the member institutions concerning health priorities, as well as coordinating activities that would contribute to the control of schistosomiasis and other diseases of public health importance.

The provision of water supply and sanitation systems is rarely the responsibility of a single governmental agency. In the context of the International Drinking Water Supply and Sanitation Decade, coordination of the provision of water supply and sanitation systems between the ministry of health and the implementing agencies could mean that these systems are installed in areas where they would have the maximum impact on the control of schistosomiasis and other water-borne diseases.

5.7 Assessment of the economic impact of schistosomiasis

Planning decisions concerning the allocation of resources to schistosomiasis control are influenced by the perceived social and economic impact of schistosomiasis. Health improvement should produce a measurable increase in the potential supply of labour available for production which should in turn eventually result in a marked increase in output in the economy. Unfortunately perhaps, it is not possible to quantify with any accuracy the impact of a disease that affects children and young adults (8).

Current knowledge does not yet provide a sufficient basis for analysing the benefits of schistosomiasis control programmes within a conventional development planning framework. Schistosomiasis control can cause measurable improvements in labour productivity but these benefits are quantifiable only in the small proportion of heavily infected persons in endemic areas. Empirical research undertaken during the last decade has clarified the conditions under which schistosomiasis control would generate significant economic benefits. The major remaining difficulty is to make quantitative predictions of the expected health benefits that would underlie these economic benefits.

From a planning perspective, therefore, the major issue is the development of quantitative methods to predict the changes in mortality and morbidity resulting from alternative control interventions. This is a prerequisite for any economic analysis.
Successful development of these methods would at least enable planners to analyse the cost-effectiveness of alternative interventions and could then, if desired, make it possible to undertake cost-benefit analyses of control programmes. Research into the mortality and morbidity indicators of the disease to determine better estimates of case fatality and disability rates is a high priority.

The direct cost of schistosomiasis to the health delivery system is another aspect of the economic impact of schistosomiasis. Heavily infected persons are at a high risk of developing disease that may eventually deplete the scarce resources available for the treatment of severe cases. If schistosomiasis is recognized by the population as being a serious disease even when there is only a light infection, outpatient services may be overburdened solely for the diagnosis and treatment of infection. No data were available to the Expert Committee on the actual direct costs of schistosomiasis to the health delivery system in any endemic country.

6. CONCLUSIONS

The objectives of schistosomiasis control are to prevent serious disease, to reduce morbidity, and to reduce transmission substantially. Improvement of the socioeconomic conditions in endemic areas provides the long-term solution to schistosomiasis control, but in these areas, and in others where water development projects exacerbate the problem, morbidity control is now feasible. The availability of the more recent antischistosomal drugs (metrifonate, oxamniquine, and praziquantel) which are safe, highly effective, and easily administered orally at the community level, provide the basis for a feasible strategy for morbidity control. Treatment reduces prevalence and the intensity of infection, prevents or reduces pathological manifestations in infected individuals, and is generally considered the most cost-effective way of achieving schistosomiasis control.

Different operational approaches are available and those that are most appropriate to a particular area must be determined at the national or local level taking into account the severity of schistosomiasis in the area, its priority rating as a public health problem, and the available resources. Active community participation and compliance are necessary to ensure that the maximum
benefits are derived from the use of chemotherapy; in particular the
treatment of children is of prime importance.

Schistosomiasis control involves two distinct phases. During the
attack phase, intensive chemotherapy will generally be carried out
jointly by specialized mobile teams and the primary health care
system, while during the maintenance phase, control should be the
responsibility of the primary health care and referral systems and
workers.

Intensive operations to reduce morbidity are of limited duration.
Therefore, a maintenance phase of transmission control is essential
so that any improvements obtained last for as long as possible. The
immigration of infected persons into an area may pose a major
problem. The re-treatment of specific population groups may
become necessary when the intensity and prevalence of infection
reach levels that predispose to serious disease.

Qualitative prevalence surveys, which may be carried out if data
are not available, are useful only to identify localities to be covered
by the programme. Before chemotherapy begins, quantitative
measurements should be made of egg output and morbidity and
these measurements should be repeated on population samples
throughout the programme.

The components for monitoring morbidity control should be
both simple and practical. They fall into two main groups: (a)
parasitological indices; and (b) clinical signs and measurements. The
former will include prevalence rates in defined age and sex groups
in representative population samples. In addition, egg output rates
should be recorded in such groups for subsequent analysis. The
monitoring of clinical indices should be, as far as possible,
quantitative. The clinical measurements made may include
assessments of the levels of haematuria, proteinuria, gastro-
esophageal bleeding, and of enlargement of the liver and spleen.
Surveillance and monitoring should be continuous processes. The
methods used to determine these clinical indices should be carefully
described so that results are standardized as much as possible.

In most endemic areas school-age children are considered the
most suitable target group to be monitored.

The monitoring of morbidity should, if possible, be evaluated by
an independent team and it is imperative that the objectives of the
monitoring process should be clearly stated. The methodology for
morbidity control should be distinguished from that of transmission
control, in which additional indices are involved.
7. RECOMMENDATIONS

7.1 General recommendations

(1) Since the publication of the report of the previous Expert Committee (19), experience with the available safe drugs suggests that the prevention, or at least the reduction, of morbidity due to schistosomiasis can become a reality. WHO should take steps to encourage and assist national control programmes by emphasizing the potential of these programmes to national and international aid and lending agencies.

(2) The Expert Committee recommends that national schistosomiasis control programmes be integrated into primary health care in line with the WHO policy of health for all by the year 2000. This will require that the control plans are coordinated with relevant government institutions concerned with, for example, planning, finance, irrigation, agriculture, water supplies, and public works.

(3) The Expert Committee noted the essential need for administrative and managerial expertise in schistosomiasis control projects. One of the major limitations to implementation is the acute shortage of qualified personnel. National governments may wish to consider long-term approaches to maintaining qualified staff. The motivation of field personnel may be enhanced by in-service training, job security, and adequate remuneration for attaining operational goals.

(4) In accordance with resolution WHA29.58 on schistosomiasis, adopted in 1976 by the Twenty-ninth World Health Assembly, the Expert Committee emphasized the importance of conducting planned epidemiological, biological, and ecological studies before the implementation of water development schemes in tropical areas in order to prevent, or at least minimize, the occurrence of adverse health effects, of which schistosomiasis is only one. WHO should continue to emphasize these concepts not only to international and national lending agencies but also to ministries of health and finance of the countries concerned. This particularly concerns the implementation of water-resource projects in West Africa in response to the disastrous Sahelian drought.

(5) While WHO has done valuable work in collaboration with Member States in the control of schistosomiasis in large man-made lakes, attention in endemic countries should also be directed to field
research on, and the prevention of, health problems arising from smaller reservoirs and irrigation schemes. These schemes frequently involve migrant workers who deserve special attention regarding both their own risk of infection and the chance that they will transmit infection to others.

(6) There is a need for continuing research on both the development and the field application of new methods of control, and special encouragement must be given to the continuing close liaison between actual control programmes and the field research and training aspects of the WHO Parasitic Diseases Programme. Basic research by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases concerning the development of new methods is encouraged.

(7) Several national schistosomiasis control programmes are now operating. Technical cooperation between established schistosomiasis programmes and newly established or proposed programmes should be encouraged.

7.2 Technical recommendations

(1) The preparation of a comprehensive “plan of action” is regarded as a basic requirement for implementing national schistosomiasis control programmes. The Expert Committee therefore strongly encouraged national health authorities of countries where schistosomiasis ranks high as a public health priority to arrange for the preparation of such an action-oriented document, which may also be used to solicit international collaboration and support when necessary.

(2) For the sound and effective maintenance of a control programme, intensification of coordination with, and active participation and support by, other government agencies is recommended, particularly agencies from the irrigation, agriculture, and public health sectors.

(3) Studies are needed to define more clearly the extent of morbidity that might be expected from the various levels of prevalence and intensity of infection of each of the major human schistosomes. This is needed so that public health administrators may decide when (or how often) intervention is needed on the basis of public health impact. The use of standardized quantitative parasitological techniques and standardized criteria for clinical evaluation to predict changes that might result from the use of
alternative control interventions would enable planners to carry out cost-effectiveness analysis.

(4) National research institutions or universities should carry out research on behalf of control programmes, to provide baseline epidemiological data and to evaluate the progress made in reducing morbidity and the transmission of schistosome infections.

(5) The newer drugs now available for schistosomiasis are adequate for the task of morbidity control, but experience with many other infectious diseases suggests that the situation may change. The Expert Committee was unanimous in its view that research by pharmaceutical companies and others with the object of developing new antischistosomal compounds should continue. It is recommended that the collaboration between WHO and the pharmaceutical industry regarding the promotion, coordination, conduct, and analysis of clinical trials in the field of parasitic diseases, be continued.

(6) At present, there is no danger of drug resistance among the schistosomes; however, since rare cases of resistance have been reported it is necessary to remain aware of this threat and further research into this problem is recommended.

(7) Although the extensive immunological studies that have been carried out have not yet had an impact on the practical aspects of schistosomiasis control, the Expert Committee recommends that research into the immunology and immunopathology of schistosomiasis should continue in order to understand the human immune response and the pathogenesis of disease before and after treatment.

(8) The Expert Committee recognizes the importance of health education and recommends that efforts be made to encourage the development of health education programmes concerning schistosomiasis that are culturally acceptable to the target community and designed to elicit both individual and community involvement.

(9) Training forms the backbone of any schistosomiasis control programme. More attention should be given to the organization of intensive training courses at the national, regional, and interregional levels.

(10) Further studies are required to improve understanding of the relationship between urinary schistosomiasis and carcinoma of the bladder, as well as to define the pathogenesis of schistosome-associated bladder cancer and to identify the predisposing factors.
(11) Increased efforts should be made to develop more precise methods for quantifying snail-host capacity to both sympatric and allopatric parasite strains. A simple technique for identifying susceptible snail hosts is needed.

(12) With special reference to the cost-effectiveness of transmission control, improved strategies and delivery systems for mollusciciding are needed. In addition, rigorous field testing of suitable, promising biological control agents, especially competitor snail species, and of new molluscicides should be encouraged.

(13) The Expert Committee endorsed the need for systematic reporting of morbidity due to schistosomiasis and recommends that the following additions be considered for inclusion in the tenth revision of the International Classification of Diseases to facilitate the reporting and assessment of global control efforts:

(a) combined hepatomegaly and splenomegaly (hepatosplenic diseases) due to schistosomiasis;
(b) hepatic fibrosis due to schistosomiasis;
(c) pulmonary arteritis due to schistosomiasis;
(d) chronic cor pulmonale due to schistosomiasis;
(e) colonic polyposis due to schistosomiasis;
(f) hydrenephrosis due to *S. haematobium* infection; and/or
(g) hydroureter;
(h) pseudo-neoplastic lesions due to schistosomiasis.

(14) Schistosomiasis is usually not among the notifiable diseases. However, systematic case reporting in endemic countries, using the International Classification of Diseases, is recommended. WHO epidemiological reporting resources may be used to facilitate the assessment of global control efforts.

ACKNOWLEDGEMENTS

The Expert Committee wishes to acknowledge the special contributions to its discussion of the following WHO staff members: Dr A.H. Aboul, Responsible Officer for Prevention and Control of Parasitic Diseases, WHO Regional Office for Africa, Brazzaville, Congo; Dr B.C. Dazo, Responsible Officer for Parasitic Diseases, WHO Regional Office for the Western Pacific, Manila, Philippines; Mr H. Dixon, Statistician, Epidemiological and Statistical Methodology, Division of Epidemiological Surveillance and Health Situation and Trend Assessment, Geneva, Switzerland; Dr G.E. Farid, Responsible Officer for Parasitic Diseases, WHO Regional Office for the Eastern Mediterranean, Alexandria, Egypt; Dr F.S.
McCullough, Scientist, Ecology and Control of Vectors, Division of Vector Biology and Control, Geneva, Switzerland.

The Expert Committee also acknowledges the valuable contributions from the following persons that helped provide a basis for the discussions and final report of the Committee: Professor M. T. Alasou, Ministry of Public Health, Rabat, Morocco; Dr A. Allen, Welsh National School of Medicine, Cardiff, Wales; Dr E. G. Beausoleil, WHO Regional Office for Africa, Brazzaville, Congo; Dr J. C. Bina, Unit of Tropical Medicine and Nutrition, University of Brasilia, Brasilia, Brazil; Dr L. Caetano da Silva, Institute of Tropical Medicine, University of Sao Paulo, Brazil; Dr A. W. Cheever, National Institutes of Health, Bethesda, MD, USA; Dr Chen Ming Gang, Institute of Parasitic Diseases, Shanghai, China; Dr K. de Cock, USC School of Medicine, Rancho Los Amigos Hospital, Downey, CA, USA; Dr D. G. Colley, Vanderbilt University School of Medicine, Nashville, TN, USA; Dr B. Elem, University Teaching Hospital, Lusaka, Zambia; Dr S. El-Maghoub, Faculty of Medicine Ain Shams, Cairo University, Cairo, Egypt; Dr A. Fenwick, Medical Research Laboratory, Khartoum, Sudan; Dr J. T. Fiusa Lima, SUCAM, Brasilia, Brazil; Dr R. Foster, Pfizer Central Research, Sandwich, Kent, England; Professor M. Gelfand, University of Zimbabwe, Harare, Zimbabwe; Dr J. M. Gentile, Hope College, Holland, MI, USA; Dr G. J. Greer, Academy of Natural Sciences of Philadelphia – Schistosomiasis Project, Institute for Medical Research, Kuala Lumpur, Malaysia; Dr M. Hayashi, Kofu City Hospital, Kofu, Japan; Dr G. Higashi, School of Public Health, University of Michigan, Ann Arbor, MI, USA; Dr R. Korte, Agency for Technical Cooperation, Federal Republic of Germany (GTZ), Eschborn, Federal Republic of Germany; Dr M. Laaziri, Ministry of Public Health, Rabat, Morocco; Dr M. C. Latham, Cornell University, Ithaca, NY, USA; Dr S. B. Lucas, School of Medicine, University College, London, England; Dr L. Lyra, Department of Clinical Medicine, Professor Edgard Santos Hospital, Salvador, Bahia, Brazil; Dr A. A. F. Mahmoud, Geographic Medicine Division, University Hospital, Cleveland, OH, USA; Dr I. Marshall, Liverpool School of Tropical Medicine, Liverpool, England; Mr A. F. Mgeni, Ministry of Health and Social Welfare, Zanzibar, United Republic of Tanzania; Dr A. B. Mobarak, Ministry of Health, Cairo, Egypt; Dr P. R. Morgan, Blair Research Laboratory, Harare, Zimbabwe; Dr R. Olveda, Research Institute for Tropical Medicine, Metro–Manila, Philippines; Mr N. Prescott, The World Bank, Washington, DC, USA; Dr L. Rey, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil; Dr D. Rollinson, British Museum (Natural History), London, England; Dr L. P. Sanchez-Longo, University of Puerto Rico, School of Medicine, San Juan, Puerto Rico; Dr A. T. Santos Jr, Department of Health, San Lazaro Hospital Compound, Manila, Philippines; Dr B. Schmidt-Ehry, Agency for Technical Cooperation, Federal Republic of Germany (GTZ), Eschborn, Federal Republic of Germany; Dr E. M. Scrimgeour, National Institutes of Health, Bethesda, MD, USA; Dr S. Sornmann, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Dr J. H. Smith, University of Texas, Medical Branch, Galveston, TX, USA; Dr L. S. Stephenson, Cornell University, Ithaca, NY, USA; Dr H. Stohler, F. Hoffmann-La Roche & Co Ltd., Basel, Switzerland; Dr H. Streibel, Ciba-Geigy Ltd., Basel, Switzerland; Dr R. F. Sturrock, London School of Hygiene and Tropical Medicine, London, England; Dr N. Tan Liu, University of the Philippines, Medical Centre, Ermita, Manila, Philippines; Professor A. Wahab, Faculty of Medicine Kaser El-Aini, Cairo University, Cairo, Egypt.
REFERENCES

Annex 1

INDICES FOR USE IN SCHISTOSOMIASIS CONTROL PROGRAMMES

The indices below are recommended for use in establishing adequate baseline information, monitoring operations, and evaluating schistosomiasis control programmes.

Indices based on egg counts

(1) Prevalence of infection: the proportion of the population with schistosomiasis, i.e., the proportion of individuals with schistosome eggs in their urine or faeces.

(2) Prevalence of heavy infections: the proportion of individuals with at least 50 eggs per 10 ml of urine for *S. haematobium* infections or with at least 100–800 eggs per gram of faeces for *S. mansoni* infections. These categories are area-specific (see Annex 2).

(3) Intensity of infection: this is estimated according to the number of eggs per unit volume of urine or weight of faeces. These data may be presented according to egg-count classes (see sections 3.2.1.1 and 3.2.2.1).

(4) Incidence: the rate at which uninfected persons who have never been treated become infected during a given period of time.

For most control programmes, it will be sufficient to calculate only indices (1) and (2). Indices (3) and (4) are more appropriate for special studies within the programme. In this case, to calculate the intensity of infection, it is recommended that a figure for the geometric mean egg output among the infected individuals is obtained as well.

Indices related to morbidity

(1) Within a stated time interval, the number of hospital beds occupied by patients with schistosomiasis infections.

(2) The number of outpatient visits related to schistosomiasis infections at dispensaries, health units, and hospitals.

110
A. *For S. haematobium* infections

(1) Proportion of persons with a recent history of haematuria and/or dysuria.

(2) Prevalence of gross haematuria at the time of examination.

(3) Prevalence of haematuria as detected by chemical reagent strips.

B. *For S. mansoni* and *S. japonicum* infections

(1) Proportion of persons with recent history of haematemesis.

(2) Prevalence of hepatic and/or splenic enlargement in schoolchildren (the presence or absence of meso- or hyperendemic malaria should be noted).

**Indices related to chemotherapy**

(1) *Participation rate*: the proportion of persons who have received treatment. Individuals who are only partially treated in schemes using a drug regime requiring more than one dose should be recorded separately.

(2) *Egg-negative rate*: the proportion of infected persons who were treated and who have no *Schistosoma* eggs in the urine or faeces at a follow-up examination. The diagnostic technique used, the interval since treatment, and the number of samples examined must be stated.

(3) *Egg-positive rate*: the proportion of people who are positive after treatment; their individual pretreatment status is unknown. These measurements should be presented according to egg-count classes. A high proportion of heavily infected persons is indicative of intensive transmission.

(4) *Reinfection rate*: this term is reserved for use in monitoring schistosomiasis control when individual data are available. The proportion of people who had no *Schistosoma* eggs at the first examination at least 3 months after treatment and who were again found to be infected at a subsequent examination after 6 months or more. This measurement should be presented according to egg-count classes. The length of time between examinations should be stated.
Annex 2

OPTIONAL CHEMOTHERAPEUTIC APPROACHES

The following approaches are suggested according to the prevalence of schistosomiasis among school-age children (7–14 years) and the type of schistosomiasis in the locality under consideration.

1. Attack phase/Intervention phase

<table>
<thead>
<tr>
<th>Risk</th>
<th>Prevalence of infection</th>
<th>Type of infection</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>&gt;50%</td>
<td>S. haematobium</td>
<td>All school-age children</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. mansoni and S. japonicum</td>
<td>All survey population</td>
</tr>
<tr>
<td>Moderate</td>
<td>25%–50%</td>
<td>S. haematobium</td>
<td>Only children aged 7–14 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. mansoni and S. japonicum</td>
<td>All children aged 2–14 years</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;25%</td>
<td>S. haematobium</td>
<td>Infected persons only through health delivery system</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. mansoni and S. japonicum</td>
<td></td>
</tr>
</tbody>
</table>

*In children 7–14 years of age.
2. Maintenance phase

<table>
<thead>
<tr>
<th>Risk</th>
<th>Prevalence of infection at follow-up</th>
<th>Proportion of heavily infected persons (%)*</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>(&gt;50%)</td>
<td>High (&gt;25)</td>
<td>All school-age children</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. haematobium</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. mansoni</em> and <em>S. japonicum</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low (&lt;25)</td>
<td><em>S. haematobium</em></td>
<td>Only 7–14-year-old children</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. mansoni</em> and <em>S. japonicum</em></td>
<td>All children aged 2–14 years</td>
</tr>
<tr>
<td>Moderate</td>
<td>(25–50%)</td>
<td>High (&gt;20)</td>
<td>Only 7–14-year-old children</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. haematobium</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. mansoni</em> and <em>S. japonicum</em></td>
<td>All children aged 2–14 years</td>
</tr>
<tr>
<td></td>
<td>Low (&lt;20)</td>
<td><em>S. haematobium</em></td>
<td>Only 7–14-year-old children</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. mansoni</em> and <em>S. japonicum</em></td>
<td>All children aged 2–14 years</td>
</tr>
<tr>
<td>Low</td>
<td>(&lt;25%)</td>
<td>High (&gt;15)</td>
<td>Primary health care at yearly intervals</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. haematobium</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. mansoni</em> and <em>S. japonicum</em></td>
<td>Primary health care at 6-month intervals</td>
</tr>
<tr>
<td></td>
<td>Low (&lt;15)</td>
<td><em>S. haematobium</em></td>
<td>Primary health care at yearly intervals</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. mansoni</em> and <em>S. japonicum</em></td>
<td></td>
</tr>
</tbody>
</table>

*The definition of heavy infection is area-specific and may vary considerably according to the epidemiology of schistosomiasis, but the following figures provide a baseline:

- *S. haematobium*: > 50 eggs per 10 ml of urine
- *S. mansoni*: > 100–800 eggs per g of faeces
- *S. intercalatum*: > 100 eggs per g of faeces
- *S. japonicum*: > 100–800 eggs per g of faeces
- *S. mekongi*: > 100 eggs per g of faeces
**Recent reports:**

<table>
<thead>
<tr>
<th>No.</th>
<th>Title</th>
<th>Pages</th>
<th>Price (Sw. fr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>670</td>
<td>Research on the menopause</td>
<td>120</td>
<td>8</td>
</tr>
<tr>
<td>671</td>
<td>Tuberculosis control</td>
<td>26</td>
<td>3</td>
</tr>
<tr>
<td>672</td>
<td>Control of vitamin A deficiency and xerophthalmia</td>
<td>70</td>
<td>7</td>
</tr>
<tr>
<td>673</td>
<td>WHO Expert Committee on Biological Standardization</td>
<td>180</td>
<td>13</td>
</tr>
<tr>
<td>674</td>
<td>Treponemal infections</td>
<td>75</td>
<td>6</td>
</tr>
<tr>
<td>675</td>
<td>Chemotherapy of leprosy for control programmes</td>
<td>33</td>
<td>4</td>
</tr>
<tr>
<td>676</td>
<td>Interferon therapy</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>677</td>
<td>Recommended health-based limits in occupational exposure to pesticides</td>
<td>110</td>
<td>8</td>
</tr>
<tr>
<td>678</td>
<td>Prevention of coronary heart disease</td>
<td>53</td>
<td>5</td>
</tr>
<tr>
<td>679</td>
<td>Biological control of vectors of disease</td>
<td>59</td>
<td>4</td>
</tr>
<tr>
<td>680</td>
<td>Malaria control and national health goals</td>
<td>68</td>
<td>6</td>
</tr>
<tr>
<td>681</td>
<td>WHO Expert Committee on Specifications for Pharmaceutical Preparations</td>
<td>33</td>
<td>4</td>
</tr>
<tr>
<td>682</td>
<td>Bacterial and viral zoonoses</td>
<td>146</td>
<td>11</td>
</tr>
<tr>
<td>683</td>
<td>Evaluation of certain food additives and contaminants</td>
<td>51</td>
<td>5</td>
</tr>
<tr>
<td>684</td>
<td>Recommended health-based occupational exposure limits for selected vegetable dusts</td>
<td>78</td>
<td>6</td>
</tr>
<tr>
<td>685</td>
<td>The use of essential drugs</td>
<td>46</td>
<td>4</td>
</tr>
</tbody>
</table>